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=> d
L1 HAS NO ANSWERS
L1                STR
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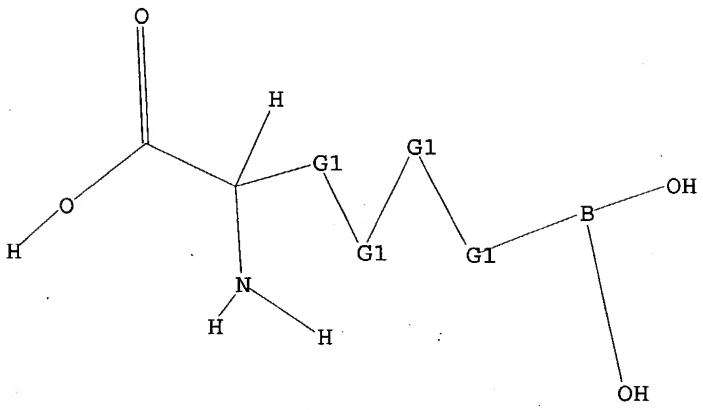

G1 CH2,O,S,N

Structure attributes must be viewed using STN Express query preparation.

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=> s l1
SAMPLE SEARCH INITIATED 12:20:43 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      31 TO ITERATE

100.0% PROCESSED       31 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          286 TO       954
PROJECTED ANSWERS:               0 TO         0

L2             0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 12:20:47 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     460 TO ITERATE

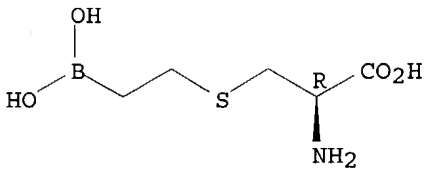
100.0% PROCESSED      460 ITERATIONS                                5 ANSWERS
SEARCH TIME: 00.00.01

L3             5 SEA SSS FUL L1

=> d 1-5

L3   ANSWER 1 OF 5  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   222638-67-7  REGISTRY
CN   L-Cysteine, S-(2-boronoethyl)-, hydrochloride (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C5 H12 B N O4 S . Cl H
SR   CA
LC   STN Files:   CA, CAPLUS, CHEMCATS, USPAT2, USPATFULL
CRN  (63107-40-4)

Absolute stereochemistry.
```

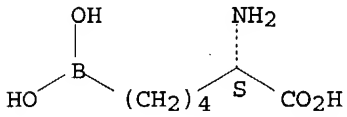


● HCl

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN
RN 222638-65-5 REGISTRY
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C6 H14 B N O4
CI COM
SR CA
LC STN Files: CA, CAPLUS, CHEMCATS, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.

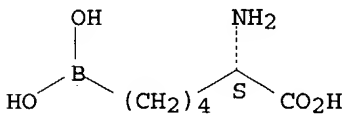


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN
RN 194656-75-2 REGISTRY
CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C6 H14 B N O4 . Cl H
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
CRN (222638-65-5)

Absolute stereochemistry.

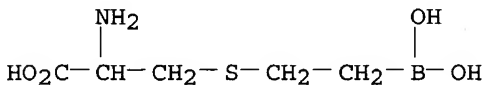


● HCl

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN

RN 88642-86-8 REGISTRY
CN Alanine, 3-[(2-boronoethyl)thio]- (7CI) (CA INDEX NAME)
OTHER NAMES:
CN NSC 77838
MF C5 H12 B N O4 S
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS
(*File contains numerically searchable property data)

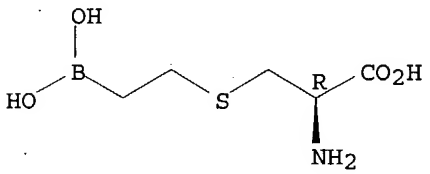


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L3 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN
RN 63107-40-4 REGISTRY
CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN S-(2-Boronoethyl)-L-cysteine
FS STEREOSEARCH
MF C5 H12 B N O4 S
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	165.53	167.00

FILE 'CAPLUS' ENTERED AT 12:22:51 ON 26 APR 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 26 Apr 2004 VOL 140 ISS 18
FILE LAST UPDATED: 25 Apr 2004 (20040425/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 14 L3

=> d ibib abs hitstr 1-14

L4 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:757815 CAPLUS
DOCUMENT NUMBER: 139:271048
TITLE: Modulation of the immune response through the manipulation of arginine levels
INVENTOR(S): Ochoa, Augusto C.; Ochoa, Juan B.; Popescu, Mircea; Zea, Arnold H.; Rodriguez, Paulo C.
PATENT ASSIGNEE(S): LSU Medical Center, USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078578	A2	20030925	WO 2003-US7523	20030312
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004057926	A1	20040325	US 2003-386131	20030312

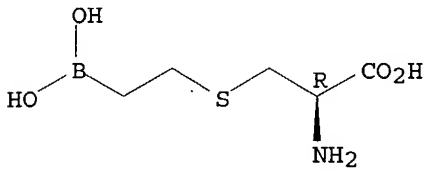
PRIORITY APPLN. INFO.: US 2002-363366P P 20020312

AB The invention provides methods and compns. for modulating an immune response by controlling the level of arginase available to a cell, tissue or system. An immune response can be enhanced or depressed by altering the amount of arginine available to a cell, tissue or system through the manipulation of localized or systemic arginine levels using substances which provide arginine to the body and enzymes which break down arginine, e.g. arginase and nitric oxide synthase. Increasing or decreasing an immune response according to the invention provides therapeutic treatment for a variety of conditions and diseases. The invention also provides clin. methods and kits which can measure the strength or resistance to an immune response in a cell, tissue or system based upon the amount of available arginine and enzymes which break down arginine.

IT **63107-40-4 222638-65-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

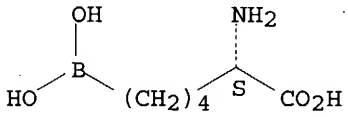
(Biological study); USES (Uses)
(arginine level manipulation for immune response modulation)
RN 63107-40-4 CAPLUS
CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 222638-65-5 CAPLUS
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

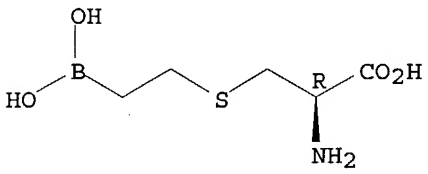
Absolute stereochemistry.



L4 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:485171 CAPLUS
DOCUMENT NUMBER: 139:175824
TITLE: Human Arginase II: Crystal Structure and Physiological Role in Male and Female Sexual Arousal
AUTHOR(S): Cama, Evis; Colleluori, Diana M.; Emig, Frances A.; Shin, Hyunshun; Kim, Soo Woong; Kim, Noel N.; Traish, Abdulmaged M.; Ash, David E.; Christianson, David W.
CORPORATE SOURCE: Roy and Diana Vagelos Laboratories Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA
SOURCE: Biochemistry (2003), 42(28), 8445-8451
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Arginase is a binuclear manganese metalloenzyme that catalyzes the hydrolysis of L-arginine to form L-ornithine and urea. The X-ray crystal structure of a fully active, truncated form of human arginase II complexed with a boronic acid transition state analog inhibitor has been determined at 2.7 Å resolution This structure is consistent with the hydrolysis of L-arginine through a metal-activated hydroxide mechanism. Given that human arginase II appears to play a role in regulating L-arginine bioavailability to NO synthase in human penile corpus cavernosum smooth muscle, the inhibition of human arginase II is a potential new strategy for the treatment of erectile dysfunction. Since NO synthase is found in human clitoral corpus cavernosum and vagina, we hypothesized that human arginase II is similarly present in these tissues and functions to regulate L-arginine bioavailability to NO synthase. Accordingly, hemodynamic studies conducted with a boronic acid arginase inhibitor in vivo are summarized, suggesting that the extrahepatic arginase plays a role in both male and female sexual arousal. Therefore, arginase II is a potential target for the treatment of male and female sexual arousal disorders.
IT **63107-40-4D**, L-Cysteine, S-(2-boronoethyl)-, complexes with arginase II
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL

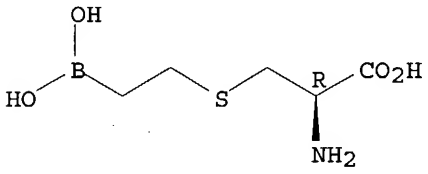
(Biological study)
(crystal structure of human arginase II complexed with boronic acid transition state analog inhibitor and physiol. role of arginase II in male and female sexual arousal)
RN 63107-40-4 CAPLUS
CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



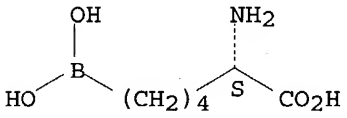
IT **63107-40-4 222638-65-5**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystal structure of human arginase II complexed with boronic acid transition state analog inhibitor and physiol. role of arginase II in male and female sexual arousal)
RN 63107-40-4 CAPLUS
CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 222638-65-5 CAPLUS
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:667433 CAPLUS
DOCUMENT NUMBER: 137:206548
TITLE: Herbal composition for inhibiting arginase and enhancing sexual response
INVENTOR(S): Heleen, Pamela A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6444237	B1	20020903	US 2001-952275	20010913

PRIORITY APPLN. INFO.: US 2001-952275 20010913

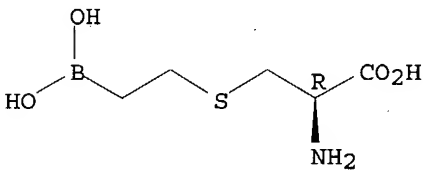
AB A unique combination of herbal ingredients designed to overcome natural inhibitors of human sexual response and allow for improved response and psychol. effects is described. The composition is comprised of exts. taken from Crataegus monogyna berry, Turnera diffusa, Pfaffia paniculata, Ginkgo biloba, Pygeum africanum, and ginsenosides extract, that are combined with L-arginine, L-glutamic acid and L-theanine in amts. effective to produce desired results. For example, a powder formulation contained L-arginine 1.5 g, L-glutamic acid 0.15 g, C. monogyna berry extract 0.08 g, T. diffusa extract 0.07 g, P. paniculata extract 0.07 g, G. biloba extract 0.06 g, P. africanum extract 0.05 g, L-theanine 0.04 g, and ginsenosides mixture 0.02 g. After oral administration (mixed with water), more pronounced sexual response was reported by a majority of participants in comparison to the com. product (Sexual Performance Enhancer).

IT **63107-40-4**, S-(2-Boronoethyl)-L-cysteine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exts.; herbal compns. for inhibiting arginase and enhancing sexual response)

RN 63107-40-4 CAPLUS

CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:367283 CAPLUS

DOCUMENT NUMBER: 136:355488

TITLE: Preparation of borono amino acids as arginase inhibitors

INVENTOR(S): Christianson, David; Baggio, Ricky; Elbaum, Daniel

PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA

SOURCE: U.S., 64 pp., Cont.-in-part of Appl. No. PCT/US98/21430.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6387890	B1	20020514	US 2000-545737	20000410
WO 9919295	A1	19990422	WO 1998-US21430	19981009
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 2003036529	A1	20030220	US 2002-53939	20020123
US 6723710	B2	20040420		
US 2004063666	A1	20040401	US 2003-661965	20030912

PRIORITY APPLN. INFO.: US 1997-61607P P 19971010
WO 1998-US21430 A2 19981009

US 2000-545737 A3 20000410
US 2002-53939 A1 20020123

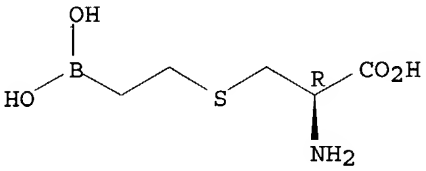
OTHER SOURCE(S): MARPAT 136:355488

AB Borono amino acids HO2CCH(NH2)-X1-X2-X3-X4-B(OH)2 (X1-X4 = CH2, S, O, NH, N-alkyl) and compns. and methods for inhibiting arginase activity using borono amino acids are described. Thus, 2(S)-amino-6-boronohexanoic acid, prepared in 5 steps from Boc-Glu-OCMe3 via conversion to the side chain aldehyde, Wittig olefination with Ph3P:CH2, hydroboration with BH3, trapping with (1S,2S,4R,6S)-(+)-pinanediol, and deprotection with BCl3, inhibited arginase with Ki = 0.1 μM.

IT **63107-40-4P 222638-65-5P 222638-67-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of borono amino acids as arginase inhibitors)

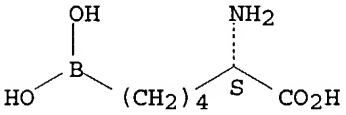
RN 63107-40-4 CAPLUS
CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



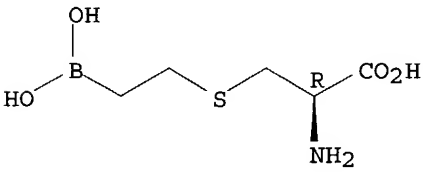
RN 222638-65-5 CAPLUS
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 222638-67-7 CAPLUS
CN L-Cysteine, S-(2-boronoethyl)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

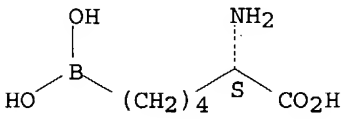


● HCl

IT **194656-75-2P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation, arginase inhibitory activity, and crystal structure of)

RN 194656-75-2 CAPLUS
CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

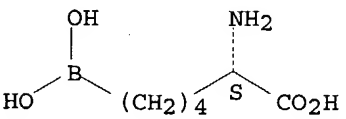
L4 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:489955 CAPLUS
DOCUMENT NUMBER: 135:223271
TITLE: Classical and Slow-Binding Inhibitors of Human Type II Arginase
AUTHOR(S): Colleluori, Diana M.; Ash, David E.
CORPORATE SOURCE: Department of Biochemistry, Temple University School of Medicine, Philadelphia, PA, 19140, USA
SOURCE: Biochemistry (2001), 40(31), 9356-9362
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Arginases catalyze the hydrolysis of L-arginine to yield L-ornithine and urea. Recent studies indicate that arginases, both the type I and type II isoenzymes, participate in the regulation of nitric oxide production by modulating the availability of arginine for nitric oxide synthase. Due to the reciprocal regulation between arginase and nitric oxide synthase, arginase inhibitors have therapeutic potential in treating nitric oxide-dependent smooth muscle disorders, such as erectile dysfunction. The authors demonstrate the competitive inhibition of the mitochondrial human type II arginase by Nω-hydroxy-L-arginine, the intermediate in the reaction catalyzed by nitric oxide synthase, and its analog Nω-hydroxy-nor-L-arginine, with Ki values of 1.6 μM and 51 nM at pH 7.5, resp. The authors also demonstrate the inhibition of human type II arginase by the boronic acid-based transition-state analogs 2(S)-amino-6-boronohexanoic acid (ABH) and S-(2-boronoethyl)-L-cysteine (BEC), which are known inhibitors of type I arginase. At pH 7.5, both ABH and BEC are classical, competitive inhibitors of human type II arginase with Ki values of 0.25 and 0.31 μM, resp. However, at pH 9.5, ABH and BEC are slow-binding inhibitors of the enzyme with Ki values of 8.5 and 30 nM, resp. The findings presented here indicate that the design of arginine analogs with uncharged, tetrahedral functional groups will lead to the development of more potent inhibitors of arginases at physiol. pH.

IT **222638-65-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(arginine analogs as classical and slow-binding inhibitors of human type II arginase)

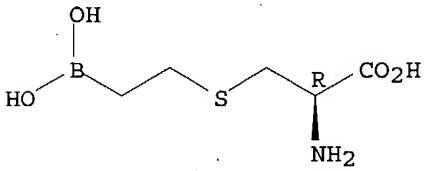
RN 222638-65-5 CAPLUS
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **63107-40-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(arginine analogs as classical and slow-binding inhibitors of human type II arginase)
RN 63107-40-4 CAPLUS
CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

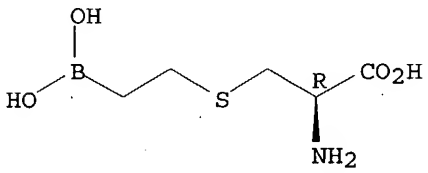


REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:78738 CAPLUS
DOCUMENT NUMBER: 134:261208
TITLE: Probing Erectile Function: S-(2-Boronoethyl)-L-Cysteine Binds to Arginase as a Transition State Analogue and Enhances Smooth Muscle Relaxation in Human Penile Corpus Cavernosum
AUTHOR(S): Kim, Noel N.; Cox, J. David; Baggio, Ricky F.; Emig, Frances A.; Mistry, Sanjay K.; Harper, Sandy L.; Speicher, David W.; Morris, Sidney M., Jr.; Ash, David E.; Traish, Abdulmaged; Christianson, David W.
CORPORATE SOURCE: Departments of Urology and Biochemistry, Boston University School of Medicine, Boston, MA, 02118, USA
SOURCE: Biochemistry (2001), 40(9), 2678-2688
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The boronic acid-based arginine analog S-(2-boronoethyl)-L-cysteine (BEC) has been synthesized and assayed as a slow-binding competitive inhibitor of the binuclear manganese metalloenzyme arginase. Kinetic measurements indicate a KI value of 0.4-0.6 μM, which is in reasonable agreement with the dissociation constant of 2.22 μM measured by isothermal titration calorimetry. The x-ray crystal structure of the arginase-BEC complex has been determined at 2.3 Å resolution from crystals perfectly twinned by hemihedry. The structure of the complex reveals that the boronic acid moiety undergoes nucleophilic attack by metal-bridging hydroxide ion to yield a tetrahedral boronate anion that bridges the binuclear manganese cluster, thereby mimicking the tetrahedral intermediate (and its flanking transition states) in the arginine hydrolysis reaction. Accordingly, the binding mode of BEC is consistent with the structure-based mechanism proposed for arginase as outlined in Cox et al. [Cox, J. D., Cama, E., Colleluori D. M., Pethe, S., Boucher, J. S., Mansuy, D., Ash, D. E., and Christianson, D. W. (2001) Biochem. 40]. Since BEC does not inhibit nitric oxide synthase, BEC serves as a valuable reagent to probe the physiol. relation between arginase and nitric oxide (NO) synthase in regulating the NO-dependent smooth muscle relaxation in human penile corpus cavernosum tissue that is required for erection. Consequently, the authors demonstrate that arginase is present in human penile corpus cavernosum tissue, and that the arginase inhibitor BEC causes significant enhancement of NO-dependent smooth muscle relaxation in this tissue. Therefore, human penile arginase is a potential target for the treatment of sexual dysfunction in the male.

IT **63107-40-4P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(boronoethylcysteine binds to arginase as a transition state analog and enhances smooth muscle relaxation in human penile corpus cavernosum in relation to probing erectile function and treatment of sexual dysfunction)
RN 63107-40-4 CAPLUS
CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

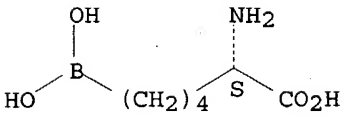
Absolute stereochemistry.



REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:13532 CAPLUS
DOCUMENT NUMBER: 132:322102
TITLE: Synthesis and evaluation of ω-borono-α-amino acids as active-site probes of arginase and nitric oxide synthases
AUTHOR(S): Collet, Sylvain; Carreaux, Francois; Boucher, Jean-Luc; Pethe, Stephanie; Lepoivre, Michel; Danion-Bougot, Renee; Danion, Daniel
CORPORATE SOURCE: UMR 6510 CNRS, Synthese et Electrosynthese organiques, Universite Rennes I, Rennes, 35042, Fr.
SOURCE: Perkin 1 (2000), (2), 177-182
CODEN: PERKF9
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Enantiomerically pure ω-borono-α-amino acids of various chain lengths have been synthesized according to a general methodol. involving condensation of alkenyl and alkynyl bromides with NiII complex of the Schiff base derived from glycine and (S)-2-[N'-(N-benzylprolyl)amino]benzophenone, hydroboration of the intermediate ω-unsatd. α-amino acids with diisopinocampheylborane, oxidation with acetaldehyde. Some of these compds. act as potent inhibitors of rat liver and murine macrophage arginases, demonstrating that distance between the B(OH)2 and α-amino acid groups is a key determinant for their interaction with arginase. In contrast, they are without effect on neuronal and inducible NO synthases.
IT **222638-65-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and evaluation of enantiopure ω-borono-α-amino acids as inhibitors of arginase and nitric oxide synthases)
RN 222638-65-5 CAPLUS
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

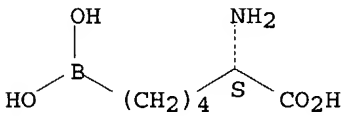
Absolute stereochemistry.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:799941 CAPLUS
DOCUMENT NUMBER: 132:148344
TITLE: A New Chromophoric Assay for Arginase Activity
AUTHOR(S): Baggio, Rick; Cox, J. David; Harper, Sandy L.; Speicher, David W.; Christianson, David W.
CORPORATE SOURCE: Roy and Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA
SOURCE: Analytical Biochemistry (1999), 276(2), 251-253
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It is reported that 1-nitro-3-guanidinobenzene (NGB) is a new assay substrate for arginase, yielding products urea plus the chromophore m-nitroaniline. The simple two-step synthesis of NGB is outlined. The authors concluded with a description of its kinetic parameters and a brief discussion of the utility of this assay. (c) 1999 Academic Press.
IT **222638-65-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(chromophoric assay for arginase activity using nitroguanidinobenzene as substrate and study of enzyme inhibition by aminoboronohexanoic acid)
RN 222638-65-5 CAPLUS
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

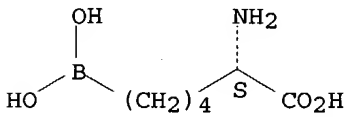
L4 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:725889 CAPLUS
DOCUMENT NUMBER: 132:76677
TITLE: Arginase-boronic acid complex highlights a physiological role in erectile function
AUTHOR(S): Cox, J. David; Kim, Noel N.; Traish, Abdulmaged M.; Christianson, David W.
CORPORATE SOURCE: Roy and Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA
SOURCE: Nature Structural Biology (1999), 6(11), 1043-1047
CODEN: NSBIEW; ISSN: 1072-8368
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The crystal structure of the complex between the binuclear manganese

metalloenzyme arginase and the boronic acid analog of L-arginine, 2(S)-amino-6-boronohexanoic acid (ABH), has been determined at 1.7 Å resolution from a crystal perfectly twinned by hemihedry. ABH binds as the tetrahedral boronate anion, with one hydroxyl oxygen sym. bridging the binuclear manganese cluster and a second hydroxyl oxygen coordinating to Mn2+A. This binding mode mimics the transition state of a metal-activated hydroxide mechanism. This transition state structure differs from that occurring in NO biosynthesis, thereby explaining why ABH does not inhibit NO synthase. We also show that arginase activity is present in the penis. Accordingly, the tight binding and specificity of ABH allows us to probe the physiol. role of arginase in modulating the NO-dependent smooth muscle relaxation required for erection. Strikingly, ABH causes significant enhancement of nonadrenergic, noncholinergic nerve-mediated relaxation of penile corpus cavernosum smooth muscle, suggesting that arginase inhibition sustains L-arginine concns. for NO synthase activity. Therefore, human penile arginase is a potential target for therapeutic intervention in the treatment of erectile dysfunction.

IT **222638-65-5D**, arginase complexes
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(arginase-boronic acid complex highlights a physiol. role in erectile function)

RN 222638-65-5 CAPLUS
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:547966 CAPLUS
DOCUMENT NUMBER: 131:295396
TITLE: Biochemical and functional profile of a newly developed potent and isozyme-selective arginase inhibitor
AUTHOR(S): Baggio, Ricky; Emig, Frances A.; Christianson, David W.; Ash, David E.; Chakder, Sushanta; Rattan, Satish
CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1999), 290(3), 1409-1416
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

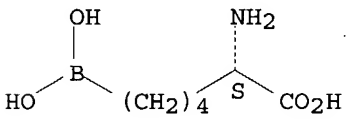
AB An increase in arginase activity has been associated with the pathophysiol. of a number of conditions, including an impairment in nonadrenergic and noncholinergic (NANC) nerve-mediated relaxation of the gastrointestinal smooth muscle. An arginase inhibitor may rectify this condition. We compared the effects of a newly designed arginase inhibitor, 2(S)-amino-6-boronohexanoic acid (ABH), with the currently available Nω-hydroxy-L-arginine (L-HO-Arg), on the NANC nerve-mediated internal anal sphincter (IAS) smooth-muscle relaxation and the arginase activity in the IAS and other tissues. Arginase caused an attenuation of the IAS smooth-muscle relaxations by NANC nerve stimulation that was

restored by the arginase inhibitors. L-HO-Arg but not ABH caused dose-dependent and complete reversal of Nω-nitro-L-arginine-suppressed IAS relaxation that was similar to that seen with L-arginine. Both ABH and L-HO-Arg caused an augmentation of NANC nerve-mediated relaxation of the IAS. In the IAS, ABH was found to be ≈250 times more potent than L-HO-Arg in inhibiting the arginase activity. L-HO-Arg was found to be 10 to 18 times more potent in inhibiting the arginase activity in the liver than in nonhepatic tissues. We conclude that arginase plays a significant role in the regulation of nitric oxide synthase-mediated NANC relaxation in the IAS. The advent of new and selective arginase inhibitors may play a significant role in the discrimination of arginase isoenzymes and have important pathophysiol. and therapeutic implications in gastrointestinal motility disorders.

IT **222638-65-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biochem. and functional profile of potent and isoenzyme-selective arginase inhibitor, 2(S)-amino-6-boronohexanoic acid)

RN 222638-65-5 CAPLUS
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:271330 CAPLUS
DOCUMENT NUMBER: 130:282369
TITLE: Preparation of borono amino acids as arginase inhibitors
INVENTOR(S): Christianson, David W.; Baggio, Ricky; Elbaum, Daniel
PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

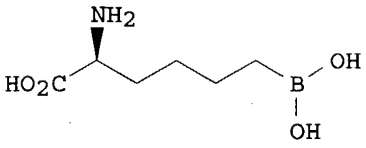
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9919295	A1	19990422	WO 1998-US21430	19981009
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2305703	AA	19990422	CA 1998-2305703	19981009
AU 9897979	A1	19990503	AU 1998-97979	19981009
EP 1049660	A1	20001108	EP 1998-952229	19981009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6387890	B1	20020514	US 2000-545737	20000410
US 2003036529	A1	20030220	US 2002-53939	20020123
US 6723710	B2	20040420		
US 2004063666	A1	20040401	US 2003-661965	20030912

PRIORITY APPLN. INFO.: US 1997-61607P P 19971010
WO 1998-US21430 W 19981009

US 2000-545737 A3 20000410
US 2002-53939 A1 20020123

OTHER SOURCE(S): MARPAT 130:282369

GI



II

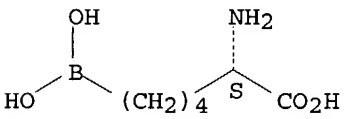
AB Title compds. HO2CCH(NH2)-Y1-Y2-Y3-Y4-B(OH)2 (I; Y1-Y4 = independently CH2, S, O, NH, N-alkyl; with the proviso that Y2 ≠ S when Y1 = Y3 = Y4 = CH2) are described. Compns. and methods for inhibiting arginase activity using I, including arginase activity in a mammal, are provided. Methods of making the compns. of the invention are also provided as are methods of using the compns. therapeutically. Thus, borono amino acid II, prepared in 5 steps from Boc-Glu-OCMe3 via conversion to the side chain aldehyde, Wittig olefination with Ph3P:CH2, hydroboration with BH3, trapping with (1S,2S,4R,6S)-(+)-pinanediol, and deprotection with BCl3, inhibited arginase with Ki = 0.1 μM.

IT **194656-75-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of borono amino acids as arginase inhibitors)

RN 194656-75-2 CAPLUS

CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



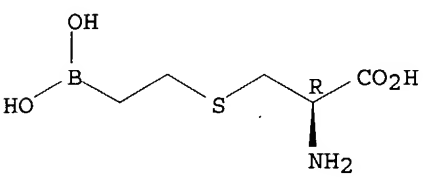
● HCl

IT **63107-40-4P 222638-65-5P 222638-67-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of borono amino acids as arginase inhibitors)

RN 63107-40-4 CAPLUS

CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

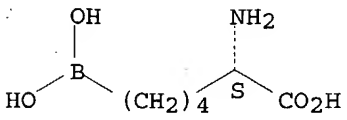
Absolute stereochemistry.



RN 222638-65-5 CAPLUS

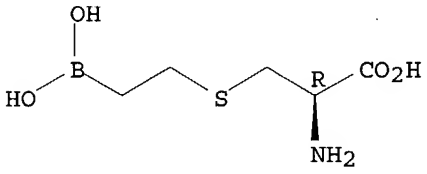
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 222638-67-7 CAPLUS
CN L-Cysteine, S-(2-boronoethyl)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:528761 CAPLUS
DOCUMENT NUMBER: 127:201930
TITLE: Inhibition of Mn2+2-arginase by borate leads to the design of a transition state analog inhibitor, 2(S)-amino-6-boronohexanoic acid
AUTHOR(S): Baggio, Ricky; Elbaum, Daniel; Kanyo, Zoltan F.; Carroll, Patrick J.; Cavalli, R. Christopher; Ash, David E.; Christianson, David W.
CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA
SOURCE: Journal of the American Chemical Society (1997), 119(34), 8107-8108
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

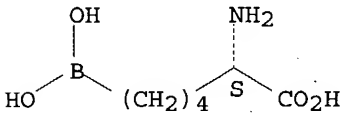
AB The tetrahedral borate anion is a modest inhibitor of Mn2+2-arginase, a critical metalloenzyme of mammalian nitrogen metabolism The crystal structure of the arginase-ornithine-borate complex reveals the net displacement of the solvent mol. bridging the binuclear manganese cluster by a borate oxygen atom in the native enzyme active site. Since this binding mode is reminiscent of the tetrahedral intermediate proposed for arginase-catalyzed arginine hydrolysis, it is postulated that a boronic acid-based arginine isostere would bind to arginase as the tetrahedral boronate anion and therefore mimic the tetrahedral intermediate and its flanking transition states in catalysis. Arginine isostere 2(S)-amino-6-boronohexanoic acid (I) was synthesized and evaluated for inhibition of arginase-catalyzed arginine hydrolysis. The results indicate that I is one of the most potent reversible inhibitors of arginase known to date with IC50 = 0.8 μM. Complete kinetic characterization of I is complicated by nonlinearity of unknown origin (there is no evidence for slow-binding behavior), but competition binding

expts. with N-hydroxyarginine indicate that Kd ≤ 0.1 μM. Based on anal. of the crystal structure of the arginase-ornithine-borate complex, a possible binding mode for I is postulated in which the metal-bridging solvent mol. observed in the native enzyme is displaced by an oxygen atom of the tetrahedral boronic acid anion.

IT **194656-75-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

RN 194656-75-2 CAPLUS
CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)

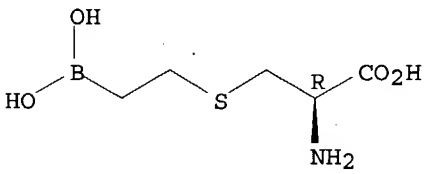
Absolute stereochemistry.



● HCl

L4 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1977:406321 CAPLUS
DOCUMENT NUMBER: 87:6321
TITLE: Preparation and evaluation of immunoglobulins labeled with S-(2-boronoethyl)cysteine
AUTHOR(S): Hartz, Thomas Peter, Jr.
CORPORATE SOURCE: Memphis State Univ., Memphis, TN, USA
SOURCE: (1976) 87 pp. Avail.: Xerox Univ. Microfilms, Ann Arbor, Mich., Order No. 77-3150
From: Diss. Abstr. Int. B 1977, 37(8), 3927-8
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **63107-40-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(labeling of immunoglobulins with, preparation and evaluation of)
RN 63107-40-4 CAPLUS
CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

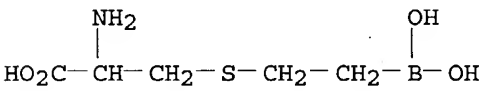


L4 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1964:461710 CAPLUS
DOCUMENT NUMBER: 61:61710
ORIGINAL REFERENCE NO.: 61:10696b-d
TITLE: Synthesis and biological evaluation of water-soluble 2-borono-ethylthio compounds

AUTHOR(S): Matteson, D. S.; Soloway, A. H.; Tomlinson, D. W.; Campbell, J. D.; Nixon, G. A.
CORPORATE SOURCE: Washington State Univ., Pullman
SOURCE: Journal of Medicinal Chemistry (1964), 7(5), 640-3
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 61:61710

AB The radical-catalyzed addition of mercaptans to the double bond of di-Bu ethyleneboronate has been employed for the synthesis of several water-soluble boronic acids. Adducts have been obtained with mercaptoacetic acid, β-mercaptopropionic acid, mercaptosuccinic acid, mercaptoethylamine hydrochloride, cysteine, mercaptoethanol, and NaHSO3. The 2-mercaptopyrimidine adduct could not be obtained directly but was prepared from di-Bu mercaptoethaneboronate and 2-chloropyrimidine. The boronic acids have been tested in C3H mice with subcutaneonsly implanted brain tumors to determine the ratio of B in the tumor to that in brain, blood, and muscle, as a function of time. One of the more favorable compds. on this basis was S-boronoethylcysteine. High transient boron ratios were found to be inadequate, and the need for binding compds. to tumor with concomitantly low B concns. in blood and brain is discussed.

IT **88642-86-8**, Alanine, 3-[(2-boronoethyl)thio]-
(preparation of)
RN 88642-86-8 CAPLUS
CN Alanine, 3-[(2-boronoethyl)thio]- (7CI) (CA INDEX NAME)



=> file beilstein

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	65.55	232.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.01	-9.01

FILE 'BEILSTEIN' ENTERED AT 12:23:25 ON 26 APR 2004

FILE RELOADED ON OCTOBER 20, 2002
FILE LAST UPDATED ON MARCH 30,2004

FILE COVERS 1771 TO 2003.
*** FILE CONTAINS 8,932,479 SUBSTANCES ***

>>> PLEASE NOTE: Reaction data and substance data are stored in separate documents and can not be searched together in one query.
Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a molecular formula or a structure search for example can be restricted to compounds with available reaction information by concatenation with PRE/FA, REA/FA or more general with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions.

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    For more detailed reaction searches BRNs can be selected from
    substance answer sets and searched in the next step as reaction
    partner BRNs - Reactant (RX.RBRN) or Product BRN (RX.PBRN).
    After a search for reaction details substance documents
    associated with reactants or products may be retrieved by
    searching RX.PBRNs or RX.RBRNs as BRNs. <<<


>>> FOR SEARCHING PREPARATIONS SEE HELP PRE  <<<

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* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.                 *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE    *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE           *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.                         *
* FOR PRICE INFORMATION SEE HELP COST                                 *
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=> d his

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L2             0 S L1
L3             5 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 12:22:51 ON 26 APR 2004
L4            14 S L3

     FILE 'BEILSTEIN' ENTERED AT 12:23:25 ON 26 APR 2004

=> s l1 full
FULL SEARCH INITIATED 12:23:32 FILE 'BEILSTEIN'
FULL SCREEN SEARCH COMPLETED -      93 TO ITERATE

100.0% PROCESSED      93 ITERATIONS                                3 ANSWERS
SEARCH TIME: 00.00.05

L5             3 SEA SSS FUL L1

=> d ide 1-3


L5   ANSWER 1 OF 3 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

     Beilstein Records (BRN):          8513901
     Chemical Name (CN):               (S)-2-Amino-6-(dihydroxyboryl)hexanoic
                                       acid hydrochloride
     Fragm. Molec. Formula (FMF):      C6 H14 B N O4 , Cl H
     Molecular Formula (MF):           C6 H14 B N O4 . Cl H
     Molecular Weight (MW):            174.99, 36.46
     Fragment BRN (FBRN):              8486411, 1098214
     Lawson Number (LN):               3808
     File Segment (FS):                Stereo compound
     Compound Type (CTYPE):            acyclic
     Constitution ID (CONSID):         7217850
     Tautomer ID (TAUTID):             8016642
     Entry Date (DED):                 2000/07/18
     Update Date (DUPD):               2000/07/18

     CM   1

     FBRN 8486411
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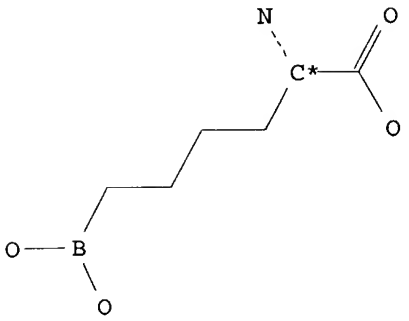
FMF C6 H14 B N O4



CM 2

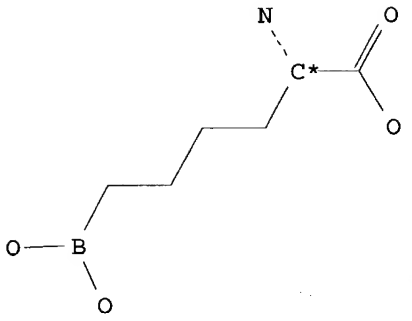
FBRN 1098214
FMF Cl H

Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
FMF	Fragment Molecular Formula	2
MF	Molecular Formula	1
FW	Formular Weight	2
FBRN	Fragment BRN	2
LN	Lawson Number	1
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
MP	Melting Point	1
NMR	Nuclear Magnetic Resonance	3

L5 ANSWER 2 OF 3 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN):	8486411
Chemical Name (CN):	(S)-2-Amino-6-(dihydroxyboryl)hexanoic acid
Molec. Formula (MF):	C6 H14 B N O4
Molecular Weight (MW):	174.99
Lawson Number (LN):	3808
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	acyclic
Constitution ID (CONSID):	7193885
Tautomer ID (TAUTID):	8001997
Entry Date (DED):	2000/07/18
Update Date (DUPD):	2000/07/18



Field Availability:

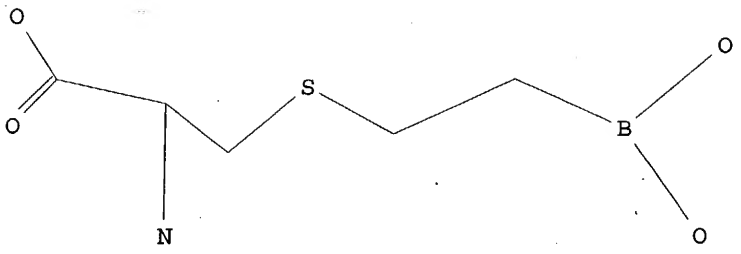
Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	1
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
MP	Melting Point	1
NMR	Nuclear Magnetic Resonance	2
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

L5 ANSWER 3 OF 3 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN):	4132291
CAS Reg. No. (RN):	63107-40-4, 88642-86-8
Chemical Name (CN):	S-(2-Borono-aethylthio)-cyctein
Molec. Formula (MF):	C5 H12 B N O4 S
Molecular Weight (MW):	193.02
Lawson Number (LN):	3813, 3544
Compound Type (CTYPE):	acyclic
Constitution ID (CONSID):	3711429
Tautomer ID (TAUTID):	3982454
Beilstein Citation (BSO):	5-04
Entry Date (DED):	1991/03/19
Update Date (DUPD):	1994/12/21



Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
RN	CAS Registry Number	2
CN	Chemical Name	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	2
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
BSO	Beilstein Citation	1
ED	Entry Date	1
UPD	Update Date	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

=> d frxpro 1-2

L5 ANSWER 1 OF 3 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

L5 ANSWER 2 OF 3 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Reaction:
RX

Reaction ID (.ID):	5352744
Reactant BRN (.RBRN):	8516325
Reactant (.RCT):	(S)-2-(tert-Butoxycarbonylamino)-6-<(1S,2S,3R,5S)-(+)-pinanyl-2,3-dioxyboryl>hexanoic acid methyl ester
Product BRN (.PBRN):	8486411
Product (.PRO):	(S)-2-Amino-6-(dihydroxyboryl)hexanoic acid
No. of React. Details (.NVAR):	1

Reaction Details:
RX

Reaction RID (.RID):	5352744.1
Reaction Classification (.CL):	Preparation
Yield (.YDT):	79 percent (BRN=8486411)
Reagent (.RGT):	HCl, H2O
Time (.TIM):	2 hour(s)

```
     Temperature (.T):                70 Cel
     Reaction Type (.TYP):            Hydrolysis
     Reference(s):
     1. Collet, Sylvain; Carreaux, Francois; Boucher, Jean-Luc; Pethe,
        Stephanie; Lepoivre, Michel; Danion-Bougot, Renee; Danion, Daniel,
        J.Chem.Soc.Perkin Trans.1, CODEN: JCPRB4(2), <2000>, 177 - 182;
        BABS-6229491


=> d his

     (FILE 'HOME' ENTERED AT 12:16:09 ON 26 APR 2004)

     FILE 'REGISTRY' ENTERED AT 12:20:29 ON 26 APR 2004
L1                STRUCTURE UPLOADED
L2              0 S L1
L3              5 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 12:22:51 ON 26 APR 2004
L4             14 S L3

     FILE 'BEILSTEIN' ENTERED AT 12:23:25 ON 26 APR 2004
L5              3 S L1 FULL
```

```
=> s arginase inhib?

          2724 ARGINASE
           113 ARGINASES
          2725 ARGINASE
                 (ARGINASE OR ARGINASES)
       1238571 INHIB?
L1          132 ARGINASE INHIB?
                 (ARGINASE(W)INHIB?)

=> s l1 and cancer

        117644 CANCER
         15808 CANCERS
        122270 CANCER
                 (CANCER OR CANCERS)
L2            1 L1 AND CANCER

=> d ibib abs


L2   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2000 ACS
ACCESSION NUMBER:         1984:622236  CAPLUS
DOCUMENT NUMBER:          101:222236
TITLE:                    Cancer therapy with chemically modified
                          enzymes. II. The therapeutic effectiveness of
                          arginase, and arginase modified by the covalent
                          attachment of polyethylene glycol, on the Taper liver
                          tumor and the L5178Y murine leukemia
AUTHOR(S):                Savoca, K. V.; Davis, F. F.; Van Es, T.; McCoy, J. R.;
                          Palczuk, N. C.
CORPORATE SOURCE:         Dep. Biol., Rutgers Univ., New Brunswick, NJ, 08903,
                          USA
SOURCE:                   Cancer Biochem. Biophys. (1984), 7(3), 261-8
                          CODEN: CABCD4; ISSN: 0305-7232
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Monomethoxypolyethylene glycol (PEG) was attached covalently to arginase;
     PEG-arginase was effective in prolonging the survival times of mice
     injected with the Taper liver tumor, whereas unmodified arginase was
     ineffective.  PEG-arginase was more effective than arginase in the in
     vitro destruction of L5178Y mouse leukemia.  However, neither PEG-arginase
     nor arginase inhibited the in vivo growth of this
     tumor.


=>  s arginase and cancer

          2724 ARGINASE
           113 ARGINASES
          2725 ARGINASE
                 (ARGINASE OR ARGINASES)
        117644 CANCER
         15808 CANCERS
        122270 CANCER
                 (CANCER OR CANCERS)
L3           41 ARGINASE AND CANCER

=> d scan


L3    41 ANSWERS   CAPLUS  COPYRIGHT 2000 ACS
IC   ICM  A61K038-50
     ICS  A61K049-00; C12N009-78; C12Q001-34
```

CC 1-12 (Pharmacology)
TI Amino acid degrading enzymes modulate cell death
ST amino acid degrading enzyme cell death modulation; cytoprotectant amino acid degrading enzyme; TNF amino acid degrading enzyme antitumor
IT Antitumor agents
Cytoprotective agents
Neuroglia
(amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNFα and inhibition of protein synthesis)
IT Tumor necrosis factors
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNFα and inhibition of protein synthesis)
IT Gene, animal
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid-degrading enzyme-encoding, transfection of; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNFα and inhibition of protein synthesis)
IT Enzymes, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid-degrading; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNFα and inhibition of protein synthesis)
IT Amino acids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enzymes degrading; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNFα and inhibition of protein synthesis)
IT Cytoprotective agents
(neuroprotectants; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNFα and inhibition of protein synthesis)
IT Transformation, genetic
(of amino acid-degrading enzyme genes; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNFα and inhibition of protein synthesis)
IT Drug screening
(of amino acid-degrading enzyme-affecting compds.; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNFα and inhibition of protein synthesis)
IT Gene therapy
(with amino acid-degrading enzyme genes; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNFα and inhibition of protein synthesis)
IT 9000-96-8, **Arginase** 9015-68-3, Asparaginase 9024-77-5, Arginine decarboxylase 9027-98-9
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNFα and inhibition of protein synthesis)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d ti 1-10

L3 ANSWER 1 OF 41 CAPLUS COPYRIGHT 2000 ACS
TI **Arginase** activity in human breast **cancer** cell lines: Nω-hydroxy-L-arginine selectively inhibits cell proliferation and induces apoptosis in MDA-MB-468 cells

L3 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2000 ACS
TI Immunohistochemical study of **arginase** in **cancer** of the stomach

L3 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2000 ACS
TI Evaluation of serum **arginase** activity in benign prostatic hypertrophy and prostatic **cancer**

L3 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2000 ACS
TI Amino acid degrading enzymes modulate cell death

L3 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2000 ACS
TI Human **arginase** II cDNA sequence, recombinant production, and use for gene therapy and clinical diagnosis

L3 ANSWER 6 OF 41 CAPLUS COPYRIGHT 2000 ACS
TI Metabolic capacity for l-citrulline synthesis from ammonia in rat isolated colonocytes

L3 ANSWER 7 OF 41 CAPLUS COPYRIGHT 2000 ACS
TI Growth inhibitory effect of L-canavanine against MIA PaCa-2 pancreatic **cancer** cells is not due to conversion to its toxic metabolite canaline

L3 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2000 ACS
TI Applications of electron paramagnetic resonance spectroscopy to study interactions of iron proteins in cells with nitric oxide

L3 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2000 ACS
TI Use of a non-mammalian DNA virus to express an exogenous gene in a mammalian cell for gene therapy in treatment of gene deficiency disorder or liver **cancer**

L3 ANSWER 10 OF 41 CAPLUS COPYRIGHT 2000 ACS
TI Extracorporeal blood treatment for systemic deprivation of amino acids in treatment of **cancer**

=> d ibib abs 2

L3 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:173162 CAPLUS
Correction of: 1996:636792
DOCUMENT NUMBER: 132:178950
Correction of: 125:324820
TITLE: Immunohistochemical study of **arginase** in **cancer** of the stomach
AUTHOR(S): Wu, Chew Wun; Chung, Wen Wei; Chi, Chin-Wen; Kao, Hwa Li; Lui, Wing Yiu; Peng, Fang-Ku; Wang, Soo Ray
CORPORATE SOURCE: Veterans General Hospital, National Yang-Ming University, Taipei, 11217, Taiwan
SOURCE: Virchows Arch. (1996), 428(6), 325-331

CODEN: VARCEM; ISSN: 0945-6317
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB High levels of **arginase** have been detected in gastric adenocarcinoma. To examine the hypothesis that this is due to macrophage infiltration into the tumor, the cellular distribution of **arginase** was localized by immunohistochem. staining. Gastric adenocarcinomas and their corresponding normal tissues (n = 46), leiomyomas (n = 2), leiomyosarcomas (n = 3), human gastric adenocarcinoma cell lines (n = 3), and benign gastric ulcers (n = 4) were examined by the avidin-biotin-peroxidase complex technique. Although macrophages with strong **arginase** immunoreactivity were observed infiltrating both gastric normal and **cancer** tissues, the data suggest the the high **arginase** levels in adenocarcinoma **cancer** tissues originate largely from **cancer** cells.

```
=> s arginase and (renal or kidney)

          2724 ARGINASE
           113 ARGINASES
          2725 ARGINASE
                 (ARGINASE OR ARGINASES)
         92639 RENAL
             7 RENALS
         92642 RENAL
                 (RENAL OR RENALS)
        177553 KIDNEY
         33592 KIDNEYS
        186263 KIDNEY
                 (KIDNEY OR KIDNEYS)
L4         378 ARGINASE AND (RENAL OR KIDNEY)

=> s l4 and arginase/ti

          1155 ARGINASE/TI
            23 ARGINASES/TI
          1173 ARGINASE/TI
                 ((ARGINASE OR ARGINASES)/TI)
L5         165 L4 AND ARGINASE/TI

=> d ti 1-10


L5   ANSWER 1 OF 165  CAPLUS  COPYRIGHT 2000 ACS
TI   Human arginase II cDNA sequence, recombinant production, and use
     for gene therapy and clinical diagnosis

L5   ANSWER 2 OF 165  CAPLUS  COPYRIGHT 2000 ACS
TI   Preparation of borono amino acids as arginase inhibitors

L5   ANSWER 3 OF 165  CAPLUS  COPYRIGHT 2000 ACS
TI   Expression of arginase II and related enzymes in the rat small
     intestine and kidney

L5   ANSWER 4 OF 165  CAPLUS  COPYRIGHT 2000 ACS
TI   Immunohistochemical localization of arginase II and other
     enzymes of arginine metabolism in rat kidney and liver

L5   ANSWER 5 OF 165  CAPLUS  COPYRIGHT 2000 ACS
TI   Identification of two arginase isoenzyme activities along the
     nephron of Meriones shawi
```

L5 ANSWER 6 OF 165 CAPLUS COPYRIGHT 2000 ACS
TI Various changes in nitric oxide synthase and **arginase** II in rat **kidney** caused by inorganic mercury

L5 ANSWER 7 OF 165 CAPLUS COPYRIGHT 2000 ACS
TI **Arginase** activity and manganese content in various tissues from control and DOCA salt-hypertensive male Sprague Dawley rats

L5 ANSWER 8 OF 165 CAPLUS COPYRIGHT 2000 ACS
TI The human **arginases** and **arginase** deficiency

L5 ANSWER 9 OF 165 CAPLUS COPYRIGHT 2000 ACS
TI Molecular cloning of cDNA for nonhepatic **arginase** (**arginase** II) and comparison of its induction with NO synthase in a murine macrophage-like cell line

L5 ANSWER 10 OF 165 CAPLUS COPYRIGHT 2000 ACS
TI **Arginase** activity is modulated by IL-4 and HOArg in nephritic glomeruli and mesangial cells

=> d arginase and erectile

'ARGINASE' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'
'AND' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'
'ERECTILE' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers; SCAN must be entered on the same line as the DISPLAY, e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, IPC, and NCL

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT) containing hit terms

```
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
              its structure diagram
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
              its structure diagram
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field
codes.  For a list of the display field codes, enter HELP DFIELDS at
an arrow prompt (=>).  Examples of formats include: TI; TI,AU; BIB,ST;
TI,IND; TI,SO.  You may specify the format fields in any order and the
information will be displayed in the same order as the format
specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR,
FHITSTR, KWIC, and OCC) may be used with DISPLAY ACC to view a
specified Accession Number.
ENTER DISPLAY FORMAT (BIB):end


=> s arginase and erectile

          2724 ARGINASE
           113 ARGINASES
          2725 ARGINASE
                  (ARGINASE OR ARGINASES)
           702 ERECTILE
L6           1 ARGINASE AND ERECTILE

=> d ti


L6   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2000 ACS
TI   Arginase-boronic acid complex highlights a physiological role in
     erectile function


=> s arginase and smooth muscle

          2724 ARGINASE
           113 ARGINASES
          2725 ARGINASE
                  (ARGINASE OR ARGINASES)
        106447 SMOOTH
           220 SMOOTHS
        106642 SMOOTH
                  (SMOOTH OR SMOOTHS)
        202740 MUSCLE
         40152 MUSCLES
        210513 MUSCLE
                  (MUSCLE OR MUSCLES)
         46944 SMOOTH MUSCLE
                  (SMOOTH(W)MUSCLE)
L7          10 ARGINASE AND SMOOTH MUSCLE

=> d ti 1-10


L7   ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2000 ACS
TI   IL-4 and IL-13 upregulate arginase I expression by cAMP and
     JAK/STAT6 pathways in vascular smooth muscle cells

L7   ANSWER 2 OF 10  CAPLUS  COPYRIGHT 2000 ACS
```

TI Progression of hepatic stellate cell activation is associated with the level of oxidative stress rather than cytokines during CCl4-induced fibrogenesis

L7 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2000 ACS
TI Enzyme immunoassay for autoantibodies to human liver-type **arginase** and its clinical application

L7 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2000 ACS
TI **Arginase**-boronic acid complex highlights a physiological role in erectile function

L7 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2000 ACS
TI Biochemical and functional profile of a newly developed potent and isozyme-selective **arginase** inhibitor

L7 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2000 ACS
TI Preparation of borono amino acids as **arginase** inhibitors

L7 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2000 ACS
TI Lysophosphatidylcholine regulates cationic amino acid transport and metabolism in vascular **smooth muscle** cells. Role in polyamine biosynthesis

L7 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2000 ACS
TI L-Arginine deficiency causes suppression of nonadrenergic noncholinergic nerve-mediated **smooth muscle** relaxation: Role of L-citrulline recycling

L7 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2000 ACS
TI Beneficial circulatory effect of L-arginine

L7 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2000 ACS
TI Identification of a 15 kilodalton actin binding region on gizzard caldesmon probed by chemical cross-linking

=> d ibib abs 4 5 7

L7 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:725889 CAPLUS
DOCUMENT NUMBER: 132:76677
TITLE: **Arginase**-boronic acid complex highlights a physiological role in erectile function
AUTHOR(S): Cox, J. David; Kim, Noel N.; Traish, Abdulmaged M.; Christianson, David W.
CORPORATE SOURCE: Roy and Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA
SOURCE: Nat. Struct. Biol. (1999), 6(11), 1043-1047
CODEN: NSBIEW; ISSN: 1072-8368
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The crystal structure of the complex between the binuclear manganese metalloenzyme **arginase** and the boronic acid analog of L-arginine, 2(S)-amino-6-boronohexanoic acid (ABH), has been determined at 1.7 Å resolution from a crystal perfectly twinned by hemihedry. ABH binds as the tetrahedral boronate anion, with one hydroxyl oxygen sym. bridging the binuclear manganese cluster and a second hydroxyl oxygen coordinating to Mn2+A. This binding mode mimics the transition state of a metal-activated hydroxide mechanism. This transition state structure differs from that occurring in NO biosynthesis, thereby explaining why ABH does not inhibit

NO synthase. We also show that **arginase** activity is present in the penis. Accordingly, the tight binding and specificity of ABH allows us to probe the physiol. role of **arginase** in modulating the NO-dependent **smooth muscle** relaxation required for erection. Strikingly, ABH causes significant enhancement of nonadrenergic, noncholinergic nerve-mediated relaxation of penile corpus cavernosum **smooth muscle**, suggesting that **arginase** inhibition sustains L-arginine concns. for NO synthase activity. Therefore, human penile **arginase** is a potential target for therapeutic intervention in the treatment of erectile dysfunction.

REFERENCE COUNT: 35

REFERENCE(S):
(1) Albina, J; J Immunol 1990, V144, P3877 CAPLUS
(3) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS
(4) Baggio, R; J Pharmacol Exp Ther 1999, V290, P1409 CAPLUS
(5) Bewley, M; Structure 1999, V7, P435 CAPLUS
(6) Brunger, A; Acta Crystallogr 1998, VD54, P905 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:547966 CAPLUS

DOCUMENT NUMBER: 131:295396

TITLE: Biochemical and functional profile of a newly developed potent and isozyme-selective **arginase** inhibitor

AUTHOR(S): Baggio, Ricky; Emig, Frances A.; Christianson, David W.; Ash, David E.; Chakder, Sushanta; Rattan, Satish

CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, USA

SOURCE: J. Pharmacol. Exp. Ther. (1999), 290(3), 1409-1416
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An increase in **arginase** activity has been associated with the pathophysiol. of a number of conditions, including an impairment in nonadrenergic and noncholinergic (NANC) nerve-mediated relaxation of the gastrointestinal **smooth muscle.** An **arginase** inhibitor may rectify this condition. We compared the effects of a newly designed **arginase** inhibitor, 2(S)-amino-6-boronohexanoic acid (ABH), with the currently available Nω-hydroxy-L-arginine (L-HO-Arg), on the NANC nerve-mediated internal anal sphincter (IAS) **smooth-muscle** relaxation and the **arginase** activity in the IAS and other tissues. **Arginase** caused an attenuation of the IAS **smooth-muscle** relaxations by NANC nerve stimulation that was restored by the **arginase** inhibitors. L-HO-Arg but not ABH caused dose-dependent and complete reversal of Nω-nitro-L-arginine-suppressed IAS relaxation that was similar to that seen with L-arginine. Both ABH and L-HO-Arg caused an augmentation of NANC nerve-mediated relaxation of the IAS. In the IAS, ABH was found to be ≈250 times more potent than L-HO-Arg in inhibiting the **arginase** activity. L-HO-Arg was found to be 10 to 18 times more potent in inhibiting the **arginase** activity in the liver than in nonhepatic tissues. We conclude that **arginase** plays a significant role in the regulation of nitric oxide synthase-mediated NANC relaxation in the IAS. The advent of new and selective **arginase** inhibitors may play a significant role in the discrimination of **arginase** isoenzymes and have important pathophysiol. and therapeutic implications in gastrointestinal motility disorders.

REFERENCE COUNT: 43

REFERENCE(S): (1) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS
(2) Biancani, P; Gastroenterology 1985, V89, P867 CAPLUS
(3) Boucher, J; Biochem Biophys Res Commun 1994, V203, P1614 CAPLUS
(4) Buga, G; Am J Physiol 1996, V271, PH1988 CAPLUS
(5) Cavalli, R; Biochemistry 1994, V33, P10652 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:775272 CAPLUS
DOCUMENT NUMBER: 128:73284
TITLE: Lysophosphatidylcholine regulates cationic amino acid transport and metabolism in vascular **smooth muscle** cells. Role in polyamine biosynthesis
AUTHOR(S): Durante, William; Liao, Lan; Peyton, Kelly J.; Schafer, Andrew I.
CORPORATE SOURCE: Houston Veterans Administration Medical Center and the Department of Medicine, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: J. Biol. Chem. (1997), 272(48), 30154-30159
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lysophosphatidylcholine (lyso-PC) is a major component of atherogenic lipids that stimulate vascular **smooth muscle** cell (SMC) proliferation. Because cationic amino acids are metabolized to growth-stimulatory polyamines, we examined whether lyso-PC regulates the transcellular transport and metabolism of cationic amino acids by vascular SMC. Treatment of SMC with lyso-PC initially (0-2 h) decreased cationic amino acid uptake, whereas longer exposures (6-24 h) progressively increased transport. Kinetic studies indicated that lyso-PC-induced inhibition was associated with a decrease in affinity for cationic amino acids, but the stimulation was mediated by an increase in transport capacity. Lyso-PC strongly induced the expression of cationic amino acid transporter-2 mRNA while modestly elevating the level of cationic amino acid transporter-1 mRNA. In addition, lyso-PC stimulated intracellular cationic amino acid metabolism by inducing ornithine decarboxylase activity and mRNA expression and also by inducing **arginase** activity in vascular SMC. In contrast, lyso-PC inhibited the catabolism of L-arginine to nitric oxide by blocking inducible nitric oxide synthase expression. Lyso-PC increased markedly the capacity of SMC to generate putrescine, a polyamine, from extracellular L-ornithine and L-arginine. The lyso-PC-mediated increase in the production of putrescine was reversed by NG-methyl-L-arginine, a competitive inhibitor of cationic amino acid transport, or by α-difluoromethylornithine, an ornithine decarboxylase inhibitor. The formation of putrescine from L-arginine was also prevented by **arginase** inhibitor NG-hydroxy-L-arginine. These results demonstrate that lyso-PC stimulates polyamine synthesis in vascular SMC by inducing the expression of the genes that regulate both the transport and metabolism of cationic amino acids. The actions of lyso-PC in stimulating cationic amino acid uptake and directing their metabolism to growth-stimulatory polyamines while simultaneously inhibiting the synthesis of antiproliferative NO, may contribute to lyso-PC-induced SMC proliferation and atherosclerotic lesion formation.

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     (FILE 'HOME' ENTERED AT 07:40:40 ON 18 AUG 2000)

     FILE 'CAPLUS' ENTERED AT 07:40:47 ON 18 AUG 2000
L1             1 S 127:201930/DN
                 SEL RN

     FILE 'REGISTRY' ENTERED AT 07:41:47 ON 18 AUG 2000
L2             8 S E1-E8
L3             1 S NORLEUCINE AND L2

     FILE 'CAPLUS' ENTERED AT 07:42:34 ON 18 AUG 2000

=> s l3 and l2

               2 L3
            2671 L2
L4             2 L3 AND L2

=> s l3 and l1

               2 L3
L5             1 L3 AND L1

=> d ibib abs hitstr it


L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2000 ACS
ACCESSION NUMBER:         1997:528761  CAPLUS
DOCUMENT NUMBER:          127:201930
TITLE:                    Inhibition of Mn2+2-arginase by borate leads to the
                          design of a transition state analog inhibitor,
                          2(S)-amino-6-boronohexanoic acid
AUTHOR(S):                Baggio, Ricky; Elbaum, Daniel; Kanyo, Zoltan F.;
                          Carroll, Patrick J.; Cavalli, R. Christopher; Ash,
                          David E.; Christianson, David W.
CORPORATE SOURCE:         Department of Chemistry, University of Pennsylvania,
                          Philadelphia, PA, 19104-6323, USA
SOURCE:                   J. Am. Chem. Soc. (1997), 119(34), 8107-8108
                          CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER:                American Chemical Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   The tetrahedral borate anion is a modest inhibitor of Mn2+2-arginase, a
     critical metalloenzyme of mammalian nitrogen metabolism  The crystal structure
of
     the arginase-ornithine-borate complex reveals the net displacement of the
     solvent mol. bridging the binuclear manganese cluster by a borate oxygen
     atom in the native enzyme active site.  Since this binding mode is
     reminiscent of the tetrahedral intermediate proposed for
     arginase-catalyzed arginine hydrolysis, it is postulated that a boronic
     acid-based arginine isostere would bind to arginase as the tetrahedral
     boronate anion and therefore mimic the tetrahedral intermediate and its
     flanking transition states in catalysis.  Arginine isostere
     2(S)-amino-6-boronohexanoic acid (I) was synthesized and evaluated for
     inhibition of arginase-catalyzed arginine hydrolysis.  The results
     indicate that I is one of the most potent reversible inhibitors of
     arginase known to date with IC50 = 0.8 μM.  Complete kinetic
     characterization of I is complicated by nonlinearity of unknown origin
     (there is no evidence for slow-binding behavior), but competition binding
     expts. with N-hydroxyarginine indicate that Kd ≤ 0.1 μM.  Based
     on anal. of the crystal structure of the arginase-ornithine-borate
     complex, a possible binding mode for I is postulated in which the
```

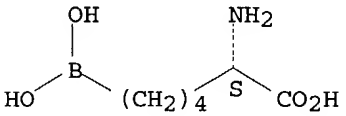
metal-bridging solvent mol. observed in the native enzyme is displaced by an oxygen atom of the tetrahedral boronic acid anion.

IT **194656-75-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

RN 194656-75-2 CAPLUS

CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

IT Enzyme inhibition kinetics
Transition state structure
(inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 24277-39-2
RL: RCT (Reactant)
(borohydride reduction during chemical synthesis; inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 11129-12-7D, Borate, complex with arginase and ornithine
RL: PRP (Properties)
(crystal structure; inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT **194656-75-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 9000-96-8, Arginase
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 90194-99-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(preparation and Swern oxidation during chemical synthesis; inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 194656-74-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(preparation and deprotection during chemical synthesis; inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 145037-74-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(preparation and hydroboration and protection during chemical synthesis;

inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 194656-73-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (preparation and reaction with triphenylphosphonium methylide during chemical synthesis; inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

```
=> s 127:201930/dn

L1            1 127:201930/DN

=> d


L1   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2000 ACS
AN   1997:528761  CAPLUS
DN   127:201930
TI   Inhibition of Mn2+2-arginase by borate leads to the design of a transition
     state analog inhibitor, 2(S)-amino-6-boronohexanoic acid
AU   Baggio, Ricky; Elbaum, Daniel; Kanyo, Zoltan F.; Carroll, Patrick J.;
     Cavalli, R. Christopher; Ash, David E.; Christianson, David W.
CS   Department of Chemistry, University of Pennsylvania, Philadelphia, PA,
     19104-6323, USA
SO   J. Am. Chem. Soc. (1997), 119(34), 8107-8108
     CODEN: JACSAT; ISSN: 0002-7863
PB   American Chemical Society
DT   Journal
LA   English


=> d it


L1   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2000 ACS
IT   Enzyme inhibition kinetics
     Transition state structure
        (inhibition of Mn2+2-arginase by borate leads to the design of
        2(S)-amino-6-boronohexanoic acid as a transition state analog
        inhibitor)
IT   24277-39-2
     RL: RCT (Reactant)
        (borohydride reduction during chemical synthesis; inhibition of
Mn2+2-arginase
        by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a
        transition state analog inhibitor)
IT   11129-12-7D, Borate, complex with arginase and ornithine
     RL: PRP (Properties)
        (crystal structure; inhibition of Mn2+2-arginase by borate leads to the
        design of 2(S)-amino-6-boronohexanoic acid as a transition state analog
        inhibitor)
IT   194656-75-2P
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); BIOL (Biological study); PREP (Preparation)
        (inhibition of Mn2+2-arginase by borate leads to the design of
        2(S)-amino-6-boronohexanoic acid as a transition state analog
        inhibitor)
IT   9000-96-8, Arginase
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (inhibition of Mn2+2-arginase by borate leads to the design of
        2(S)-amino-6-boronohexanoic acid as a transition state analog
        inhibitor)
IT   90194-99-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (preparation and Swern oxidation during chemical synthesis; inhibition of
        Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-
        boronohexanoic acid as a transition state analog inhibitor)
IT   194656-74-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (preparation and deprotection during chemical synthesis; inhibition of
        Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-
```

boronohexanoic acid as a transition state analog inhibitor)
IT 145037-74-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(preparation and hydroboration and protection during chemical synthesis; inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)
IT 194656-73-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(preparation and reaction with triphenylphosphonium methylide during chemical
synthesis; inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

=> sel rn

E1 THROUGH E8 ASSIGNED

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	3.29	3.44

FILE 'REGISTRY' ENTERED AT 07:41:47 ON 18 AUG 2000
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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 11, 2000

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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=> s e1-e8

1 11129-12-7/BI
(11129-12-7/RN)
1 145037-74-7/BI
(145037-74-7/RN)
1 194656-73-0/BI
(194656-73-0/RN)
1 194656-74-1/BI
(194656-74-1/RN)
1 194656-75-2/BI
(194656-75-2/RN)
1 24277-39-2/BI
(24277-39-2/RN)
1 9000-96-8/BI
(9000-96-8/RN)
1 90194-99-3/BI
(90194-99-3/RN)
L2 8 (11129-12-7/BI OR 145037-74-7/BI OR 194656-73-0/BI OR 194656-74-1/BI OR 194656-75-2/BI OR 24277-39-2/BI OR 9000-96-8/BI OR 90194-99-3/BI)

=> d scan

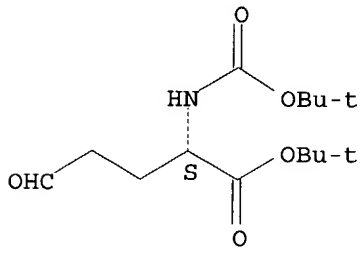
L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Arginase (9CI)
MF Unspecified
CI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

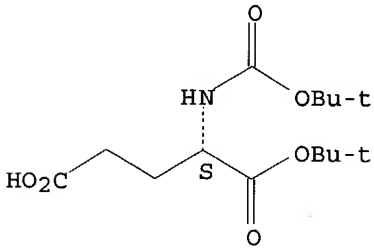
L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Norvaline, N-[(1,1-dimethylethoxy)carbonyl]-5-oxo-, 1,1-dimethylethyl ester (9CI)
MF C14 H25 N O5

Absolute stereochemistry.



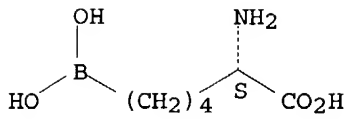
L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-, 1-(1,1-dimethylethyl) ester (9CI)
MF C14 H25 N O6
CI COM

Absolute stereochemistry. Rotation (-).



L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Norleucine, 6-borono-, hydrochloride (9CI)
MF C6 H14 B N O4 . Cl H

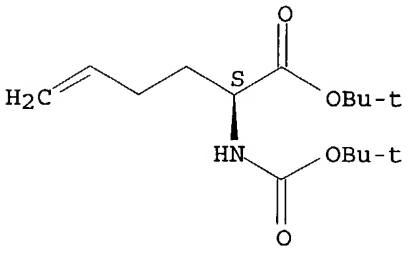
Absolute stereochemistry.



● HCl

L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN 5-Hexenoic acid, 2-[[(1,1-dimethylethoxy)carbonyl]amino]-, 1,1-dimethylethyl ester, (2S)- (9CI)
MF C15 H27 N O4

Absolute stereochemistry.

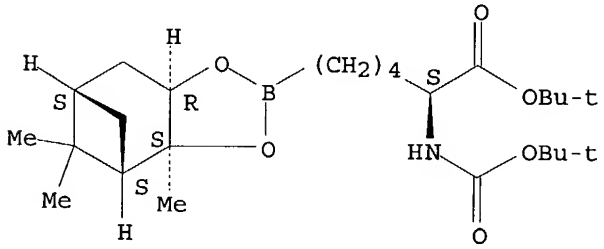


L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Borate (9CI)
MF Unspecified
CI COM, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

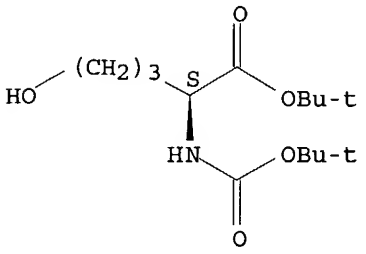
L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN 4,6-Methano-1,3,2-benzodioxaborole-2-hexanoic acid, α-[[(1,1-dimethylethoxy)carbonyl]amino]hexahydro-3a,5,5-trimethyl-, 1,1-dimethylethyl ester, (αS,3aS,4S,6S,7aR)- (9CI)
MF C25 H44 B N O6

Absolute stereochemistry.



L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Norvaline, N-[(1,1-dimethylethoxy)carbonyl]-5-hydroxy-, 1,1-dimethylethyl ester (9CI)
MF C14 H27 N O5

Absolute stereochemistry.



ALL ANSWERS HAVE BEEN SCANNED

=> s norleucine and l2

5538 NORLEUCINE
L3 1 NORLEUCINE AND L2

```
=> s assay and arginase inhibitor antagonist

        215913 ASSAY
         90055 ASSAYS
        280098 ASSAY
                 (ASSAY OR ASSAYS)
          2722 ARGINASE
           113 ARGINASES
          2723 ARGINASE
                 (ARGINASE OR ARGINASES)
        323535 INHIBITOR
        346141 INHIBITORS
        528717 INHIBITOR
                 (INHIBITOR OR INHIBITORS)
        108645 ANTAGONIST
         75126 ANTAGONISTS
        142659 ANTAGONIST
                 (ANTAGONIST OR ANTAGONISTS)
             0 ARGINASE INHIBITOR ANTAGONIST
                 (ARGINASE(W)INHIBITOR(W)ANTAGONIST)
L1           0 ASSAY AND ARGINASE INHIBITOR ANTAGONIST

=> s assay and arginase inhibitor

        215913 ASSAY
         90055 ASSAYS
        280098 ASSAY
                 (ASSAY OR ASSAYS)
          2722 ARGINASE
           113 ARGINASES
          2723 ARGINASE
                 (ARGINASE OR ARGINASES)
        323535 INHIBITOR
        346141 INHIBITORS
        528717 INHIBITOR
                 (INHIBITOR OR INHIBITORS)
            39 ARGINASE INHIBITOR
                 (ARGINASE(W)INHIBITOR)
L2           3 ASSAY AND ARGINASE INHIBITOR

=> d ibib abs hitstr 1-3


L2   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2000 ACS
ACCESSION NUMBER:        1999:500684  CAPLUS
DOCUMENT NUMBER:         132:62184
TITLE:                   Functional and molecular characterization of nitric
                         oxide synthase in the endometrium and myometrium of
                         pregnant sheep during the last third of gestation
AUTHOR(S):               Massmann, G. Angela; Zhang, Jie; Figueroa, Jorge P.
CORPORATE SOURCE:        Perinatal Research Laboratory, Departments of
                         Obstetrics and Gynecology, Wake Forest University
                         School of Medicine, Winston-Salem, NC, 27157, USA
SOURCE:                  Am. J. Obstet. Gynecol. (1999), 181(1), 116-125
                         CODEN: AJOGAH; ISSN: 0002-9378
PUBLISHER:               Mosby, Inc.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   This study was undertaken to characterize the biochem. and expression
     profiles of the nitric oxide synthase isoforms present in the sheep uterus
     during late gestation.  Myometrium and endometrium were obtained from 28
     time-mated pregnant sheep that were under halothane general anesthesia.
     Tissues were kept frozen at -80°C until they were homogenized for
     the measurement of (1) nitric oxide synthase activity according to the
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carbon 14-labeled arginine-citrulline conversion **assay**, (2) nitric oxide synthase protein mass according to Western blot anal., and (3) nitric oxide synthase mRNA according to the RNase protection **assay.** The nitric oxide synthase activity **assay** included 8 parallel treatments for biochem. characterization, in particular with the **arginase inhibitors** ornithine and (+)-S-2-amino-5-iodoacetamidopentanoic acid. The biochem. characterization of nitric oxide synthase indicated that the predominant form of nitric oxide synthase in endometrium and myometrium (80%-90%) was calcium-calmodulin dependent. In endometrium 50% of reduced NAD-dependent arginine metabolism was accounted for by the presence of alternative arginine metabolic pathways. Expressions of type 1 and type 3 nitric oxide synthase were demonstrated in endometrium and myometrium by Western blot and RNase protection **assay.** Although no significant decrease in nitric oxide synthase activity or protein mass was observed, a significant decrease in myometrial type 1 nitric oxide synthase mRNA occurred in sheep not in labor at 140 days' gestation ($P < 0.05$ by anal. of variance; term is 144 ± 5 days). In the gravid sheep uterus the predominant nitric oxide synthase isoforms are type 1 in myometrium and type 3 in endometrium. Despite a decrease in type 1 nitric oxide synthase mRNA, enzymic activity and type 1 nitric oxide synthase protein mass do not decrease before parturition.

REFERENCE COUNT: 26

REFERENCE(S):
(1) Balon, T; J Appl Physiol 1997, V82, P359 CAPLUS
(2) Bansal, R; J Clin Invest 1997, V99, P2502 CAPLUS
(3) Bradford, M; Anal Biochem 1976, V72, P248 CAPLUS
(4) Dong, Y; Biol Reprod 1998, V59, P933 CAPLUS
(5) Dong, Y; J Reprod Fertil 1996, V107, P249 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 3 CAPLUS

ACCESSION NUMBER: 1998:524033 CAPLUS
DOCUMENT NUMBER: 129:199627
TITLE: An improved **assay** for measurement of nitric oxide synthase activity in biological tissues

AUTHOR(S): Giraldez, Roberto R.; Zweier, Jay L.
CORPORATE SOURCE: Molecular and Cellular Biophysics Laboratories, Department of Medicine, Division of Cardiology, The Johns Hopkins Medical Institutions, Baltimore, MD, 21224, USA

SOURCE: Anal. Biochem. (1998), 261(1), 29-35
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB While the L-arginine conversion **assay** has been utilized to measure nitric oxide synthase (NOS) activity in isolated enzyme and pure cell prepns., this method often fails to provide accurate measurements in whole tissues. Biol. tissues contain variable amts. of unlabeled substrate and enzymes are present which can compete for substrate or independently form the product L-citrulline. NOS-independent conversion of radiolabeled L-arginine to L-citrulline occurs due to arginase- and ornithine transcarbamylase-mediated reactions and this limits the accuracy of this **assay** for measurement of NOS activity. In heart tissue, NOS-independent L-citrulline formation was observed which could not be blocked by the NOS inhibitor L-NAME but was blocked by the **arginase inhibitor** L-ornithine. To eliminate the effect of arginase-mediated L-citrulline formation, KCl-washed membrane particulate fractions were obtained by high-speed centrifugation. While arginase-mediated nonspecific activity was 85% concentrated in the cytosol, 93% of NOS activity was localized within the particulate fraction of the heart. The remaining arginase activity found in the crude pellet was mostly removed by a one-step KCl wash purification and when incubation periods of 8 min were utilized specific and accurate measurements of NOS activity

were obtained. NOS enzymic properties were defined for rat heart prepns. with a Km of 2.9 μM for L-arginine. All NOS activity detected was calcium-dependent suggesting it originated from the constitutive endothelial isoform. Thus, NOS-independent activity can be largely eliminated from the heart tissue by assaying KCl-washed membrane particulate fractions and this enables accurate quantitation of NOS activity. (c) 1998 Academic Press.

L2 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1980:619227 CAPLUS
DOCUMENT NUMBER: 93:219227
TITLE: Mechanism of action of mouse macrophages as antitumor effector cells: role of arginase
AUTHOR(S): Farram, E.; Nelson, D. S.
CORPORATE SOURCE: Kolling Inst. Med. Res., R. North Shore Hosp. Sydney, St. Leonards, 2065, Australia
SOURCE: Cell. Immunol. (1980), 55(2), 283-93
CODEN: CLIMB8; ISSN: 0008-8749
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cytotoxic macrophages, enriched by centrifugation through Percoll gradients, were obtained from the peritoneal cavities of mice bearing a tumor or injected i.p. with proteose peptone. Damage to target tumor cells was detected in microcytotoxicity **assays** and by inhibition of uptake of tritiated thymidine. Supernatants from cultured macrophages were cytotoxic. Cytotoxicity was inhibited by arginine, by the **arginase inhibitors** uric acid and adenosine, and by cyclic AMP, hydrocortisone, chloroquin, cytochalasin B, and colchicine, but not by cycloheximide, puromycin, mitomycin C, or actinomycin D; it was enhanced by indomethacin. Macrophages which were cytotoxic in vitro were also capable of suppressing tumor growth in vivo. The role of arginase secretion by macrophages in mediating this tumor cytotoxicity is discussed.

```
=> s arginase inhibitor

          2722 ARGINASE
           113 ARGINASES
          2723 ARGINASE
                 (ARGINASE OR ARGINASES)
        323535 INHIBITOR
        346141 INHIBITORS
        528717 INHIBITOR
                 (INHIBITOR OR INHIBITORS)
L3          39 ARGINASE INHIBITOR
                 (ARGINASE(W)INHIBITOR)

=> s l3 and muscle

        202673 MUSCLE
         40144 MUSCLES
        210444 MUSCLE
                 (MUSCLE OR MUSCLES)
L4           3 L3 AND MUSCLE

=> d ibib abs 1-3
```

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:547966 CAPLUS
DOCUMENT NUMBER: 131:295396
TITLE: Biochemical and functional profile of a newly developed potent and isozyme-selective

arginase inhibitor

AUTHOR(S): Baggio, Ricky; Emig, Frances A.; Christianson, David W.; Ash, David E.; Chakder, Sushanta; Rattan, Satish

CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, USA

SOURCE: J. Pharmacol. Exp. Ther. (1999), 290(3), 1409-1416
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An increase in arginase activity has been associated with the pathophysiol. of a number of conditions, including an impairment in nonadrenergic and noncholinergic (NANC) nerve-mediated relaxation of the gastrointestinal smooth **muscle.** An **arginase inhibitor** may rectify this condition. We compared the effects of a newly designed **arginase inhibitor**, 2(S)-amino-6-boronohexanoic acid (ABH), with the currently available Nω-hydroxy-L-arginine (L-HO-Arg), on the NANC nerve-mediated internal anal sphincter (IAS) smooth-**muscle** relaxation and the arginase activity in the IAS and other tissues. Arginase caused an attenuation of the IAS smooth-**muscle** relaxations by NANC nerve stimulation that was restored by the **arginase inhibitors.** L-HO-Arg but not ABH caused dose-dependent and complete reversal of Nω-nitro-L-arginine-suppressed IAS relaxation that was similar to that seen with L-arginine. Both ABH and L-HO-Arg caused an augmentation of NANC nerve-mediated relaxation of the IAS. In the IAS, ABH was found to be ≈250 times more potent than L-HO-Arg in inhibiting the arginase activity. L-HO-Arg was found to be 10 to 18 times more potent in inhibiting the arginase activity in the liver than in nonhepatic tissues. We conclude that arginase plays a significant role in the regulation of nitric oxide synthase-mediated NANC relaxation in the IAS. The advent of new and selective **arginase inhibitors** may play a significant role in the discrimination of arginase isoenzymes and have important pathophysiol. and therapeutic implications in gastrointestinal motility disorders.

REFERENCE COUNT: 43

REFERENCE(S):
(1) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS
(2) Biancani, P; Gastroenterology 1985, V89, P867 CAPLUS
(3) Boucher, J; Biochem Biophys Res Commun 1994, V203, P1614 CAPLUS
(4) Buga, G; Am J Physiol 1996, V271, PH1988 CAPLUS
(5) Cavalli, R; Biochemistry 1994, V33, P10652 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:271330 CAPLUS

DOCUMENT NUMBER: 130:282369

TITLE: Preparation of borono amino acids as **arginase inhibitors**

INVENTOR(S): Christianson, David W.; Baggio, Ricky; Elbaum, Daniel

PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA

SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

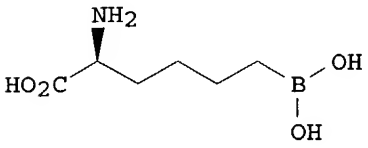
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9919295	A1	19990422	WO 1998-US21430	19981009
W: AU, CA, JP, US				

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AU 9897979	A1	19990503	AU 1998-97979	19981009
PRIORITY APPLN. INFO.:			US 1997-61607	19971010
			WO 1998-US21430	19981009

OTHER SOURCE(S): MARPAT 130:282369

GI



II

AB Title compds. HO2CCH(NH2)-Y1-Y2-Y3-Y4-B(OH)2 (I; Y1-Y4 = independently CH2, S, O, NH, N-alkyl; with the proviso that Y2 ≠ S when Y1 = Y3 = Y4 = CH2) are described. Compns. and methods for inhibiting arginase activity using I, including arginase activity in a mammal, are provided. Methods of making the compns. of the invention are also provided as are methods of using the compns. therapeutically. Thus, borono amino acid II, prepared in 5 steps from Boc-Glu-OCMe3 via conversion to the side chain aldehyde, Wittig olefination with Ph3P:CH2, hydroboration with BH3, trapping with (1S,2S,4R,6S)-(+)-pinanediol, and deprotection with BCl3, inhibited arginase with Ki = 0.1 μM.

REFERENCE COUNT: 2

REFERENCE(S):
(1) Baggio, R; J Am Chem Soc 1997
(2) Denniel, V; Tetrahedron Lett 1996

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:775272 CAPLUS

DOCUMENT NUMBER: 128:73284

TITLE: Lysophosphatidylcholine regulates cationic amino acid transport and metabolism in vascular smooth **muscle** cells. Role in polyamine biosynthesis

AUTHOR(S): Durante, William; Liao, Lan; Peyton, Kelly J.; Schafer, Andrew I.

CORPORATE SOURCE: Houston Veterans Administration Medical Center and the Department of Medicine, Baylor College of Medicine, Houston, TX, 77030, USA

SOURCE: J. Biol. Chem. (1997), 272(48), 30154-30159
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lysophosphatidylcholine (lyso-PC) is a major component of atherogenic lipids that stimulate vascular smooth **muscle** cell (SMC) proliferation. Because cationic amino acids are metabolized to growth-stimulatory polyamines, we examined whether lyso-PC regulates the transcellular transport and metabolism of cationic amino acids by vascular SMC. Treatment of SMC with lyso-PC initially (0-2 h) decreased cationic amino acid uptake, whereas longer exposures (6-24 h) progressively increased transport. Kinetic studies indicated that lyso-PC-induced inhibition was associated with a decrease in affinity for cationic amino acids, but the stimulation was mediated by an increase in transport capacity. Lyso-PC strongly induced the expression of cationic amino acid transporter-2 mRNA while modestly elevating the level of cationic amino acid transporter-1 mRNA. In addition, lyso-PC stimulated intracellular cationic amino acid metabolism by inducing ornithine decarboxylase activity and mRNA expression and also by inducing arginase activity in vascular

SMC. In contrast, lyso-PC inhibited the catabolism of L-arginine to nitric oxide by blocking inducible nitric oxide synthase expression. Lyso-PC increased markedly the capacity of SMC to generate putrescine, a polyamine, from extracellular L-ornithine and L-arginine. The lyso-PC-mediated increase in the production of putrescine was reversed by NG-methyl-L-arginine, a competitive inhibitor of cationic amino acid transport, or by α-difluoromethylornithine, an ornithine decarboxylase inhibitor. The formation of putrescine from L-arginine was also prevented by **arginase inhibitor** NG-hydroxy-L-arginine. These results demonstrate that lyso-PC stimulates polyamine synthesis in vascular SMC by inducing the expression of the genes that regulate both the transport and metabolism of cationic amino acids. The actions of lyso-PC in stimulating cationic amino acid uptake and directing their metabolism to growth-stimulatory polyamines while simultaneously inhibiting the synthesis of antiproliferative NO, may contribute to lyso-PC-induced SMC proliferation and atherosclerotic lesion formation.

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         215913 ASSAY
          90055 ASSAYS
L5       280098 ASSAY
                (ASSAY OR ASSAYS)

=> s l5 and muscle

         202673 MUSCLE
          40144 MUSCLES
         210444 MUSCLE
                (MUSCLE OR MUSCLES)
L6         7011 L5 AND MUSCLE

=> s arginase

           2722 ARGINASE
            113 ARGINASES
L7         2723 ARGINASE
                (ARGINASE OR ARGINASES)

=> s l6 and l7

L8            2 L6 AND L7

=> d ibib abs 1-2


L8   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2000 ACS
ACCESSION NUMBER:         2000:466757  CAPLUS
TITLE:                    Progression of hepatic stellate cell activation is
                          associated with the level of oxidative stress rather
                          than cytokines during CCl4-induced fibrogenesis
AUTHOR(S):                Kim, Ki-Yong; Choi, Inpyo; Kim, Soung-Soo
CORPORATE SOURCE:         Protein Laboratory, Mogam Biotechnology Research
                          Institute, Kyonggi-Do, 449-910, S. Korea
SOURCE:                   Mol. Cells (2000), 10(3), 289-300
                          CODEN: MOCEEK; ISSN: 1016-8478
PUBLISHER:                Springer-Verlag Singapore Pte. Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   In order to identify a fibrogenic factor associated with the potential of
     hepatic stellate cells (HSC) activation that arises during the
     CCl4-induced fibrogenic process, the relationship between the activation
```

of HSC and levels of several fibrogenic factors were investigated. After isolation of HSC from the liver at different stages of CCl4 intoxication, the activation of HSC was assessed by the expression of α-smooth **muscle** actin. Levels of cytokines and oxidative stress in liver homogenates and plasma were measured by enzyme linked immunosorbent **assay** and the colorimetric method. In primary culture, HSC isolated from a rat liver were gradually activated in a time-dependent manner according to CCl4 administration. The progression of HSC activation was closely correlated with parameters related to oxidative stress in liver homogenates rather than the tissue levels of several cytokines. Also, the levels of antioxidants and **arginase** activity were inversely correlated with HSC activation. In plasma, the levels of oxidative stress and cytokines in CCl4-treated rat livers were not associated with the activation of HSC found during the CCl4-induced fibrogenic process. The relationship between HSC activation and oxidative stress was also confirmed through several factor-treated HSC cultures. In conclusion, the activation of HSC was accelerated according to CCl4 administration, and the progression of HSC activation is absolutely related to the oxidative stress. These results show that enhanced oxidative stress is an important signal for activation of HSC in exptl. liver fibrogenesis.

REFERENCE COUNT: 66

REFERENCE(S):
(3) Barrett, E; Am J Physiol 1999, V276, PL979 CAPLUS
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(5) Belyaev, N; Hepatology 1992, V15, P525 CAPLUS
(6) Bonizzi, G; Biochem Pharmacol 2000, V59, P7 CAPLUS
(7) Bredt, D; Proc Natl Acad Sci USA 1990, V87, P682 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 2000:398234 CAPLUS

TITLE: Enzyme immunoassay for autoantibodies to human liver-type **arginase** and its clinical application

AUTHOR(S): Kimura, Masahiro; Tatsumi, Ke-Ita; Tada, Hisato; Ikemoto, Masaki; Fukuda, Yoshihiro; Kaneko, Akira; Kato, Michio; Hidaka, Yoh; Amino, Nobuyuki

CORPORATE SOURCE: Department of Laboratory Medicine, Osaka University Medical School, Osaka, 565-0871, Japan

SOURCE: Clin. Chem. (Washington, D. C.) (2000), 46(1), 112-117
CODEN: CLCHAU; ISSN: 0009-9147

PUBLISHER: American Association for Clinical Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: **Arginase** is an enzyme of the urea cycle, and one of the two isoenzymes is the liver-type enzyme. We examined serum autoantibodies to this liver-type enzyme in patients with hepatitis. Methods: Antibodies to recombinant human liver-type **arginase** were measured by ELISA in 95 patients and 55 healthy controls. Results: The mean absorbance values in the ELISA **assays** of patients with definite autoimmune hepatitis (n = 11; P <0.0001), probable autoimmune hepatitis (n = 31; P <0.0001), and hepatitis C (HCV; n = 20; P <0.01) were significantly different from those of healthy controls, but the values in patients with hepatitis B (HBV; n = 23) and other autoimmune diseases (n = 10) were not significantly different from those of healthy controls. When the cutoff was fixed at the upper 95th percentile of the absorbance value in healthy controls, pos. reactions were found in 18.2%, 32.3%, 20.0%, 13.0%, and 10.0% of patients with definite autoimmune hepatitis, probable autoimmune hepatitis, HCV hepatitis, HBV hepatitis, and other autoimmune diseases, resp. All of these pos. reactions were abolished by inhibition of serum with recombinant antigen. The specificity and sensitivity of this ELISA were 96% and 29%, resp. The intraassay and interassay coeffs.

of variation were 2.3-7.5% and 9.8-11%, resp. There was no relationship between these antibodies and anti-nuclear, anti-smooth **muscle**, or anti-cytochrome P450IID6 antibodies. Conclusions: The ELISA for anti-liver-type **arginase** autoantibody improved the detectability of autoimmune hepatitis when compared with established **assays** for liver-specific autoantibodies.

REFERENCE COUNT: 26

REFERENCE(S):
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(4) Glass, R; J Biol Chem 1973, V248, P5785 CAPLUS
(5) Gotoh, T; Biochem Biophys Res Commun 1997, V233, P487 CAPLUS
(6) Gotoh, T; FEBS Lett 1996, V395, P119 CAPLUS
(7) Haraguchi, Y; Proc Natl Acad Sci 1987, V84, P412 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s arginase inhibitor

```
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           113 ARGINASES
          2723 ARGINASE
                 (ARGINASE OR ARGINASES)
        323535 INHIBITOR
        346141 INHIBITORS
        528717 INHIBITOR
                 (INHIBITOR OR INHIBITORS)
L9          39 ARGINASE INHIBITOR
                 (ARGINASE(W)INHIBITOR)
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=> d ti 1-10

L9 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI L-arginine availability modulates local nitric oxide production and parasite killing in experimental trypanosomiasis

L9 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Characterization of nitric oxide synthase activity in the tropical sea anemone Aiptasia pallida

L9 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Effects of the New **Arginase Inhibitor** Nω-Hydroxy-nor-L-Arginine on NO Synthase Activity in Murine Macrophages

L9 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Biochemical and functional profile of a newly developed potent and isozyme-selective **arginase inhibitor**

L9 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Functional and molecular characterization of nitric oxide synthase in the endometrium and myometrium of pregnant sheep during the last third of gestation

L9 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Preparation of borono amino acids as **arginase inhibitors**

L9 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI L-Arginine uptake and metabolism by lung macrophages and neutrophils following intratracheal instillation of silica in vivo

L9 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI An improved assay for measurement of nitric oxide synthase activity in biological tissues

L9 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Method and formulation of stimulating nitric oxide synthesis

L9 ANSWER 10 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI α-Difluoromethylornithine (DFMO) as a potent arginase activity inhibitor in human colon carcinoma cells

=> d ti 11-39

L9 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Arginase modulates nitric oxide production in activated macrophages

L9 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Anti-MHV3 state induced by IFN gamma in macrophages is not related to arginine metabolism

L9 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Effects of L-valine on growth and polyamine metabolism in human colon carcinoma cells

L9 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Lysophosphatidylcholine regulates cationic amino acid transport and metabolism in vascular smooth muscle cells. Role in polyamine biosynthesis

L9 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Determination of nitric oxide synthase activity in rat, pig and rabbit prostate glands

L9 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Reduction of hair growth by **arginase inhibitors**

L9 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Nitric oxide synthase and arginase in cells isolated from the rat gastric mucosa

L9 ANSWER 18 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Preparation of arylamidinohydrazones for treatment of cachexia and nitric oxide-mediated diseases.

L9 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Antifertility effects of (+)-S-2-amino-6-iodoacetamidohexanoic acid (2-AIHA) in female rats

L9 ANSWER 20 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Nω-hydroxyamino-α-amino acids as a new class of very strong inhibitors of arginases

L9 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Synthesis and effects on arginase and nitric oxide synthase of two novel analogs of Nω-hydroxyarginine, Nω-hydroxyindospicine and p-hydroxyamidinophenylalanine

L9 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Inhibition of arginase by NG-hydroxy-L-arginine in alveolar macrophages: implications for the utilization of L-arginine for nitric oxide synthesis

L9 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Nω-hydroxy-L-arginine, an intermediate in the L-arginine to nitric oxide pathway, is a strong inhibitor of liver and macrophage arginase

L9 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Antitumor effect and toxicity of two new active-site-directed irreversible ornithine decarboxylase and extrahepatic **arginase inhibitors**

L9 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Arginase as one of the inhibitory principles in the density-dependent as well as plasma membrane-mediated inhibition of liver cell growth in vivo

L9 ANSWER 26 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI The presence of an **arginase inhibitor** in the hemolymph of blowfly, Aldrichina grahami, after the larva stops eating

L9 ANSWER 27 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Mechanism of action of mouse macrophages as antitumor effector cells: role of arginase

L9 ANSWER 28 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Characteristics of arginases from plant, ureotelic, and uricotelic organisms

L9 ANSWER 29 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Arginase activity during the development of Rana terrestris tadpoles

L9 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Existence of hepatic **arginase inhibitors** in several tissues

L9 ANSWER 31 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI **Arginase inhibitor** from sunflower seeds: purification and inhibitory properties

L9 ANSWER 32 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Probable physiological role of an **arginase inhibitor** in uricotelic animal liver

L9 ANSWER 33 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Arginase inhibition of dialysable factor(s) from chick liver

L9 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Inhibitory factor(s) of arginase occurring in pigeon liver

L9 ANSWER 35 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Preliminary identification of the **arginase inhibitor** from sunflower seeds

L9 ANSWER 36 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Purification, properties, and inhibition of plant agrinase

L9 ANSWER 37 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Microbiological and biochemical changes in sheep cheese

L9 ANSWER 38 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Relative depletion of an arginine-rich deoxyribonucleohistone component during tumor induction by the Shope papilloma virus

L9 ANSWER 39 OF 39 CAPLUS COPYRIGHT 2000 ACS
TI Inhibitory factor(s) of rat liver arginase occurring in chick liver

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        210444 MUSCLE
                 (MUSCLE OR MUSCLES)
L10           3 L9 AND MUSCLE

=> d ti 1-3


L10  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2000 ACS
TI   Biochemical and functional profile of a newly developed potent and
     isozyme-selective arginase inhibitor

L10  ANSWER 2 OF 3  CAPLUS  COPYRIGHT 2000 ACS
TI   Preparation of borono amino acids as arginase inhibitors

L10  ANSWER 3 OF 3  CAPLUS  COPYRIGHT 2000 ACS
TI   Lysophosphatidylcholine regulates cationic amino acid transport and
     metabolism in vascular smooth muscle cells. Role in polyamine
     biosynthesis


=> d ibib abs 1 3


L10  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2000 ACS
ACCESSION NUMBER:         1999:547966  CAPLUS
DOCUMENT NUMBER:          131:295396
TITLE:                    Biochemical and functional profile of a newly
                          developed potent and isozyme-selective
                          arginase inhibitor
AUTHOR(S):                Baggio, Ricky; Emig, Frances A.; Christianson, David
                          W.; Ash, David E.; Chakder, Sushanta; Rattan, Satish
CORPORATE SOURCE:         Department of Chemistry, University of Pennsylvania,
                          Philadelphia, PA, USA
SOURCE:                   J. Pharmacol. Exp. Ther. (1999), 290(3), 1409-1416
                          CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER:                American Society for Pharmacology and Experimental
                          Therapeutics
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   An increase in arginase activity has been associated with the pathophysiol.
     of a number of conditions, including an impairment in nonadrenergic and
     noncholinergic (NANC) nerve-mediated relaxation of the gastrointestinal
     smooth muscle. An arginase inhibitor may
     rectify this condition. We compared the effects of a newly designed
     arginase inhibitor, 2(S)-amino-6-boronohexanoic acid
     (ABH), with the currently available Nω-hydroxy-L-arginine
     (L-HO-Arg), on the NANC nerve-mediated internal anal sphincter (IAS)
     smooth-muscle relaxation and the arginase activity in the IAS
     and other tissues. Arginase caused an attenuation of the IAS smooth-
     muscle relaxations by NANC nerve stimulation that was restored by
     the arginase inhibitors. L-HO-Arg but not ABH caused
     dose-dependent and complete reversal of Nω-nitro-L-arginine-
     suppressed IAS relaxation that was similar to that seen with L-arginine.
     Both ABH and L-HO-Arg caused an augmentation of NANC nerve-mediated
     relaxation of the IAS. In the IAS, ABH was found to be ≈250 times
     more potent than L-HO-Arg in inhibiting the arginase activity. L-HO-Arg
     was found to be 10 to 18 times more potent in inhibiting the arginase
     activity in the liver than in nonhepatic tissues. We conclude that
     arginase plays a significant role in the regulation of nitric oxide
     synthase-mediated NANC relaxation in the IAS. The advent of new and
     selective arginase inhibitors may play a significant
     role in the discrimination of arginase isoenzymes and have important
     pathophysiol. and therapeutic implications in gastrointestinal motility
```

disorders.
REFERENCE COUNT: 43
REFERENCE(S):
(1) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS
(2) Biancani, P; Gastroenterology 1985, V89, P867 CAPLUS
(3) Boucher, J; Biochem Biophys Res Commun 1994, V203, P1614 CAPLUS
(4) Buga, G; Am J Physiol 1996, V271, PH1988 CAPLUS
(5) Cavalli, R; Biochemistry 1994, V33, P10652 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:775272 CAPLUS
DOCUMENT NUMBER: 128:73284
TITLE: Lysophosphatidylcholine regulates cationic amino acid transport and metabolism in vascular smooth **muscle** cells. Role in polyamine biosynthesis
AUTHOR(S): Durante, William; Liao, Lan; Peyton, Kelly J.; Schafer, Andrew I.
CORPORATE SOURCE: Houston Veterans Administration Medical Center and the Department of Medicine, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: J. Biol. Chem. (1997), 272(48), 30154-30159
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lysophosphatidylcholine (lyso-PC) is a major component of atherogenic lipids that stimulate vascular smooth **muscle** cell (SMC) proliferation. Because cationic amino acids are metabolized to growth-stimulatory polyamines, we examined whether lyso-PC regulates the transcellular transport and metabolism of cationic amino acids by vascular SMC. Treatment of SMC with lyso-PC initially (0-2 h) decreased cationic amino acid uptake, whereas longer exposures (6-24 h) progressively increased transport. Kinetic studies indicated that lyso-PC-induced inhibition was associated with a decrease in affinity for cationic amino acids, but the stimulation was mediated by an increase in transport capacity. Lyso-PC strongly induced the expression of cationic amino acid transporter-2 mRNA while modestly elevating the level of cationic amino acid transporter-1 mRNA. In addition, lyso-PC stimulated intracellular cationic amino acid metabolism by inducing ornithine decarboxylase activity and mRNA expression and also by inducing arginase activity in vascular SMC. In contrast, lyso-PC inhibited the catabolism of L-arginine to nitric oxide by blocking inducible nitric oxide synthase expression. Lyso-PC increased markedly the capacity of SMC to generate putrescine, a polyamine, from extracellular L-ornithine and L-arginine. The lyso-PC-mediated increase in the production of putrescine was reversed by NG-methyl-L-arginine, a competitive inhibitor of cationic amino acid transport, or by α-difluoromethylornithine, an ornithine decarboxylase inhibitor. The formation of putrescine from L-arginine was also prevented by **arginase inhibitor** NG-hydroxy-L-arginine. These results demonstrate that lyso-PC stimulates polyamine synthesis in vascular SMC by inducing the expression of the genes that regulate both the transport and metabolism of cationic amino acids. The actions of lyso-PC in stimulating cationic amino acid uptake and directing their metabolism to growth-stimulatory polyamines while simultaneously inhibiting the synthesis of antiproliferative NO, may contribute to lyso-PC-induced SMC proliferation and atherosclerotic lesion formation.

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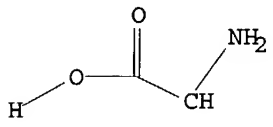

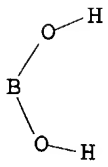

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FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 173 TO 747
PROJECTED ANSWERS: 4 TO 200

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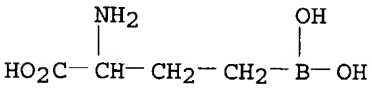

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L2 4 ANSWERS REGISTRY COPYRIGHT 2000 ACS
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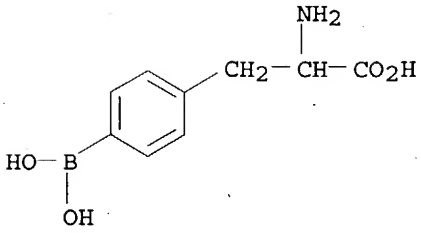
CI PMS

CM 1



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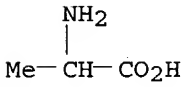
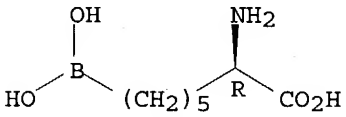


L2 4 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Heptanoic acid, 2-amino-7-borono-, (R)- (9CI)
MF C7 H16 B N O4

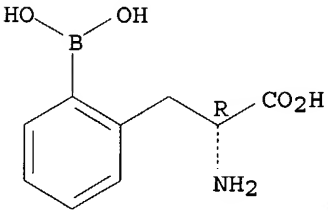
Absolute stereochemistry.



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L2 4 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN D-Phenylalanine, 2-borono- (9CI)
MF C9 H12 B N O4

Absolute stereochemistry.



ALL ANSWERS HAVE BEEN SCANNED

=> s l1 full

FULL SEARCH INITIATED 10:17:12 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 408 TO ITERATE

100.0% PROCESSED 408 ITERATIONS 56 ANSWERS
SEARCH TIME: 00.00.01

L3 56 SEA SSS FUL L1

=> s l3 and 1-10/nr

13701012 1-10/NR
L4 37 L3 AND 1-10/NR

=> d l3 not l4

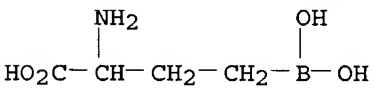
L4 IS NOT VALID HERE
For an explanation, enter "HELP DISPLAY".

=> s l3 not l4

L5 19 L3 NOT L4

=> d scan

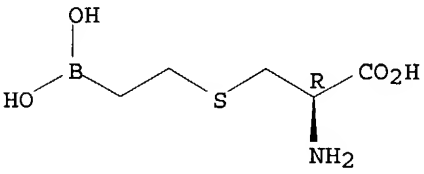
L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Butanoic acid, 2-amino-4-borono- (9CI)
MF C4 H10 B N O4
CI COM



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Cysteine, S-(2-boronoethyl)-, hydrochloride (9CI)
MF C5 H12 B N O4 S . Cl H

Absolute stereochemistry.



● HCl

L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS

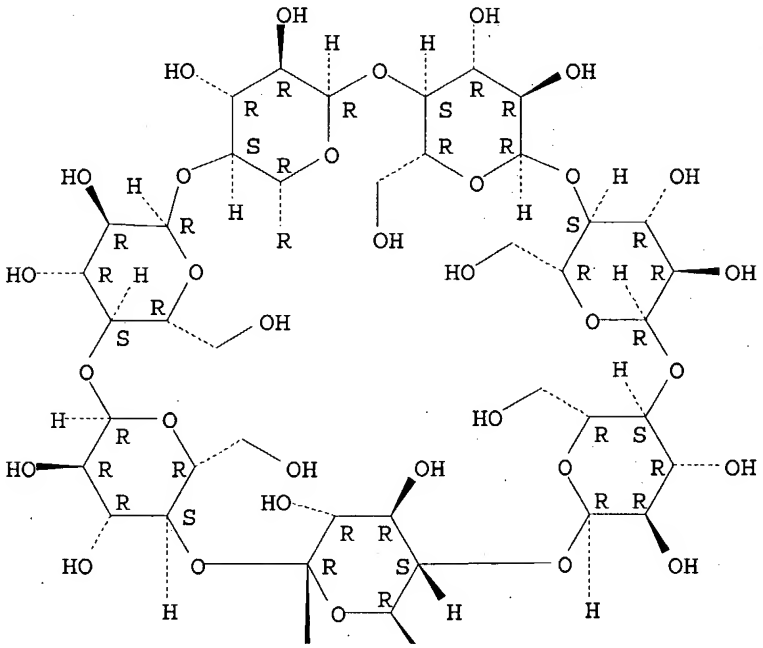
IN L-Phenylalanine, 4-borono-, compd. with O-α-D-glucopyranosyl-(1→4)-O-α-D-glucopyranosyl-(1→6A)-β-cyclodextrin (1:2) (9CI)

MF C54 H90 O45 . 1/2 C9 H12 B N O4

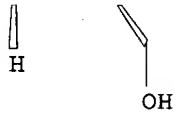
CM 1

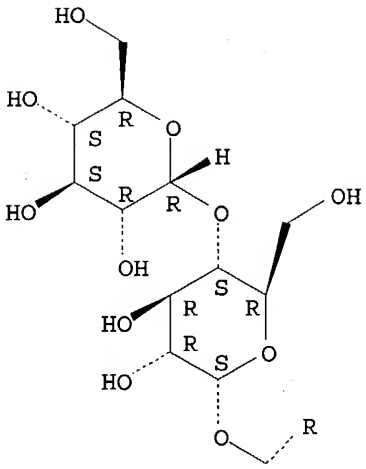
Absolute stereochemistry.

PAGE 1-A



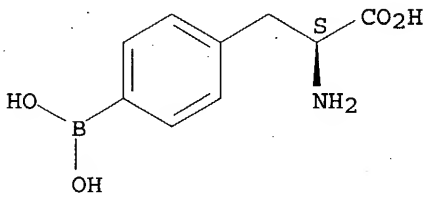
PAGE 2-A





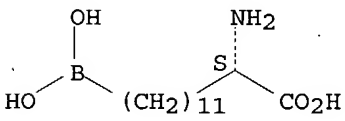
CM 2

Absolute stereochemistry. Rotation (-).



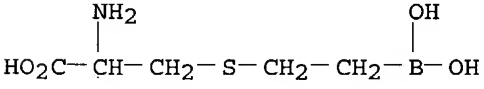
L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Tridecanoic acid, 2-amino-13-borono-, hydrochloride, (2S)- (9CI)
MF C13 H28 B N O4 . Cl H

Absolute stereochemistry.



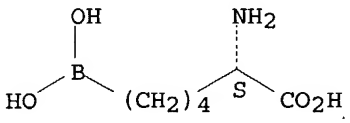
● HCl

L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Alanine, 3-[(2-boronoethyl)thio]- (7CI)
MF C5 H12 B N O4 S



L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Norleucine, 6-borono-, hydrochloride (9CI)
MF C6 H14 B N O4 . Cl H

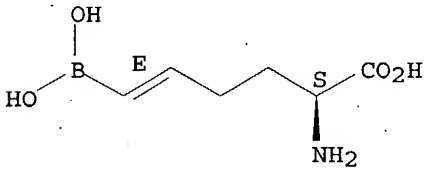
Absolute stereochemistry.



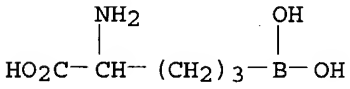
● HCl

L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN 5-Hexenoic acid, 2-amino-6-borono-, (2S,5E)- (9CI)
MF C6 H12 B N O4

Absolute stereochemistry.
Double bond geometry as shown.



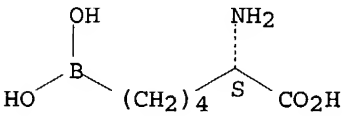
L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Norvaline, 5-borono-, hydrochloride (9CI)
MF C5 H12 B N O4 . Cl H



● HCl

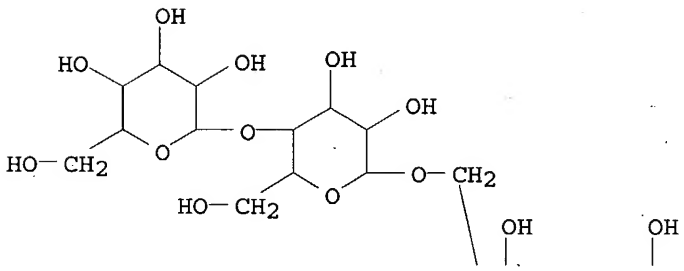
L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Norleucine, 6-borono- (9CI)
MF C6 H14 B N O4
CI COM

Absolute stereochemistry.

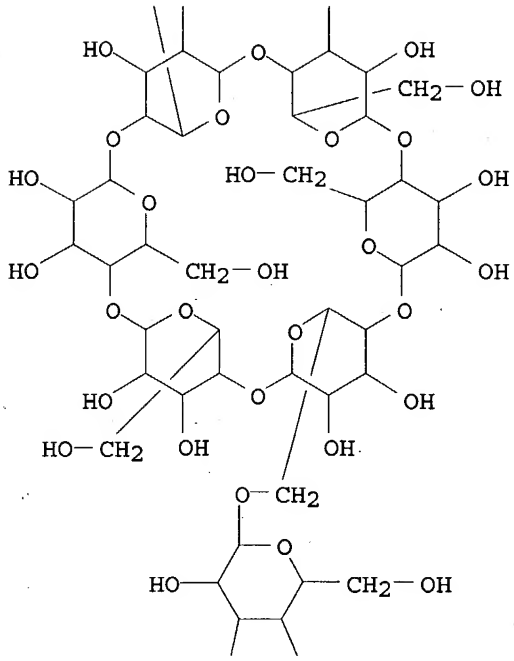


L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Phenylalanine, 4-borono-, compd. with O-α-D-glucopyranosyl-(1→4)-O-α-D-glucopyranosyl-(1→6A)-O-[O-α-D-glucopyranosyl-(1→4)-α-D-glucopyranosyl-(1→6D)]-α-cyclodextrin (1:2) (9CI)
MF C60 H100 O50 . 1/2 C9 H12 B N O4

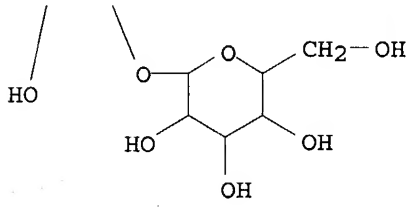
CM 1



PAGE 2-A

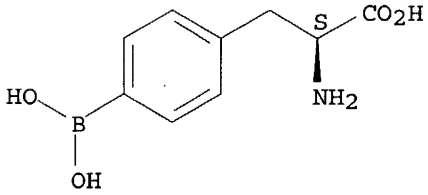


PAGE 3-A



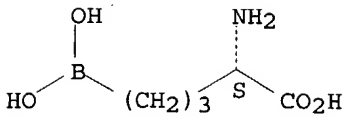
CM 2

Absolute stereochemistry. Rotation (-).



L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Norvaline, 5-borono-, hydrochloride (9CI)
MF C5 H12 B N O4 . Cl H

Absolute stereochemistry.

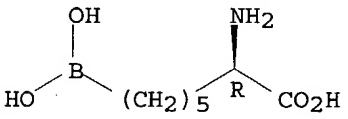


● HCl

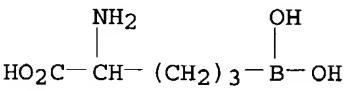
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Heptanoic acid, 2-amino-7-borono-, (R)- (9CI)
MF C7 H16 B N O4

Absolute stereochemistry.

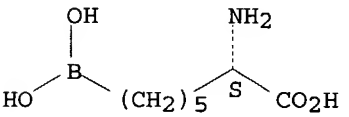


L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Norvaline, 5-borono- (9CI)
MF C5 H12 B N O4
CI COM

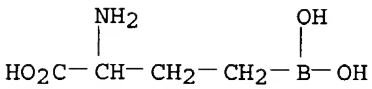


L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Heptanoic acid, 2-amino-7-borono-, (2S)- (9CI)
MF C7 H16 B N O4

Absolute stereochemistry.



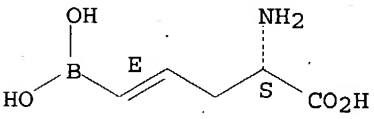
L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Butanoic acid, 2-amino-4-borono-, hydrochloride (9CI)
MF C4 H10 B N O4 . Cl H



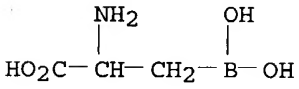
● HCl

L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN 4-Pentenoic acid, 2-amino-5-borono-, (2S,4E)- (9CI)
MF C5 H10 B N O4

Absolute stereochemistry.
Double bond geometry as shown.

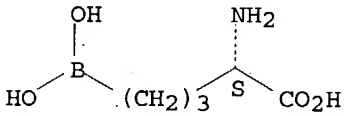


L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Alanine, 3-borono- (9CI)
MF C3 H8 B N O4



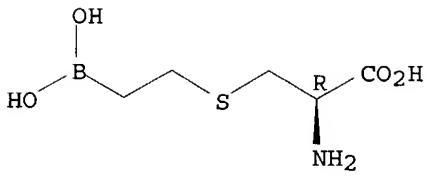
L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Norvaline, 5-borono- (9CI)
MF C5 H12 B N O4
CI COM

Absolute stereochemistry.



L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Cysteine, S-(2-boronoethyl)- (9CI)
MF C5 H12 B N O4 S
CI COM

Absolute stereochemistry.



ALL ANSWERS HAVE BEEN SCANNED

=> s l5 not Pentenoic

```
          17453 PENTENOIC
L6           18 L5 NOT PENTENOIC
```

=> s l6 not glucopyranosyl

```
         101851 GLUCOPYRANOSYL
L7           16 L6 NOT GLUCOPYRANOSYL
```

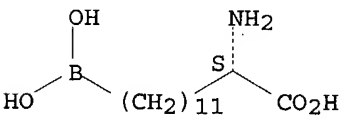
=> s l7 not Hexenoic

```
          12923 HEXENOIC
L8           15 L7 NOT HEXENOIC
```

=> d scan

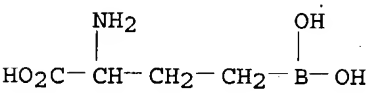
L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Tridecanoic acid, 2-amino-13-borono-, hydrochloride, (2S)- (9CI)
MF C13 H28 B N O4 . Cl H

Absolute stereochemistry.



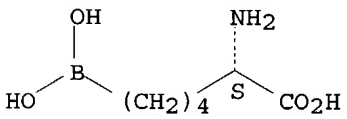
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Butanoic acid, 2-amino-4-borono-, hydrochloride (9CI)
MF C4 H10 B N O4 . Cl H

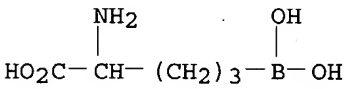


L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Norleucine, 6-borono- (9CI)
MF C6 H14 B N O4
CI COM

Absolute stereochemistry.



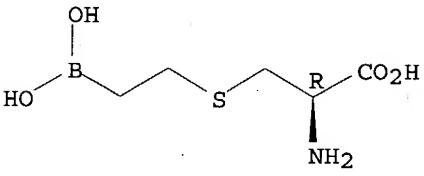
L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Norvaline, 5-borono-, hydrochloride (9CI)
MF C5 H12 B N O4 . Cl H



● HCl

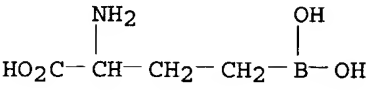
L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Cysteine, S-(2-boronoethyl)-, hydrochloride (9CI)
MF C5 H12 B N O4 S . Cl H

Absolute stereochemistry.



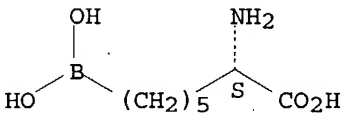
● HCl

L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Butanoic acid, 2-amino-4-borono- (9CI)
MF C4 H10 B N O4
CI COM

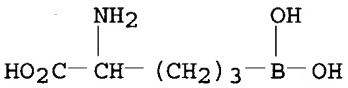


L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Heptanoic acid, 2-amino-7-borono-, (2S)- (9CI)
MF C7 H16 B N O4

Absolute stereochemistry.

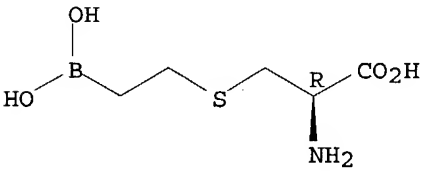


L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Norvaline, 5-borono- (9CI)
MF C5 H12 B N O4
CI COM



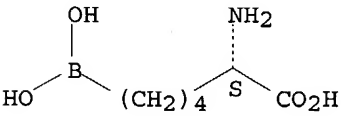
L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Cysteine, S-(2-boronoethyl)- (9CI)
MF C5 H12 B N O4 S
CI COM

Absolute stereochemistry.



L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Norleucine, 6-borono-, hydrochloride (9CI)
MF C6 H14 B N O4 . Cl H

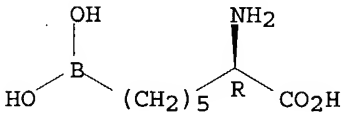
Absolute stereochemistry.



● HCl

L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Heptanoic acid, 2-amino-7-borono-, (R)- (9CI)
MF C7 H16 B N O4

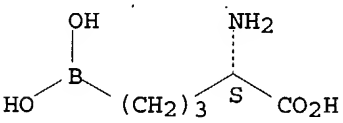
Absolute stereochemistry.



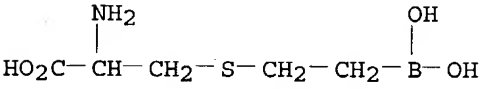
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Norvaline, 5-borono- (9CI)
MF C5 H12 B N O4
CI COM

Absolute stereochemistry.

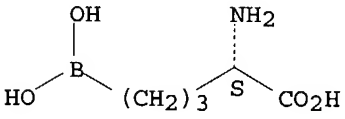


L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Alanine, 3-[(2-boronoethyl)thio]- (7CI)
MF C5 H12 B N O4 S

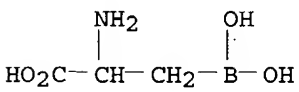


L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN L-Norvaline, 5-borono-, hydrochloride (9CI)
MF C5 H12 B N O4 . Cl H

Absolute stereochemistry.



L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS
IN Alanine, 3-borono- (9CI)
MF C3 H8 B N O4



ALL ANSWERS HAVE BEEN SCANNED

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	143.10	143.25

FILE 'CAPLUS' ENTERED AT 10:21:00 ON 16 AUG 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1967 - 16 Aug 2000 VOL 133 ISS 8
FILE LAST UPDATED: 15 Aug 2000 (20000815/ED)

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=> s l8

L9 12 L8

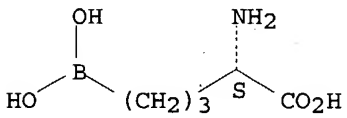
=> d ibib abs hitstr 1-12

L9 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:13532 CAPLUS
DOCUMENT NUMBER: 132:322102
TITLE: Synthesis and evaluation of ω-borono-α-amino acids as active-site probes of arginase and nitric oxide synthases
AUTHOR(S): Collet, Sylvain; Carreaux, Francois; Boucher, Jean-Luc; Pethe, Stephanie; Lepoivre, Michel;

Danion-Bougot, Renee; Danion, Daniel
CORPORATE SOURCE: UMR 6510 CNRS, Synthese et Electrosynthese organiques, Universite Rennes I, Rennes, 35042, Fr.
SOURCE: Perkin 1 (2000), (2), 177-182
CODEN: PERKF9
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Enantiomerically pure ω-borono-α-amino acids of various chain lengths have been synthesized according to a general methodol. involving condensation of alkenyl and alkynyl bromides with NiII complex of the Schiff base derived from glycine and (S)-2-[N'-(N-benzylprolyl)amino]benzophenone, hydroboration of the intermediate ω-unsatd. α-amino acids with diisopinocampheylborane, oxidation with acetaldehyde. Some of these compds. act as potent inhibitors of rat liver and murine macrophage arginases, demonstrating that distance between the B(OH)2 and α-amino acid groups is a key determinant for their interaction with arginase. In contrast, they are without effect on neuronal and inducible NO synthases.

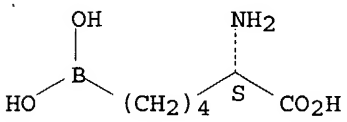
IT **212839-30-0**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(synthesis and evaluation of enantiopure ω-borono-α-amino acids as inhibitors of arginase and nitric oxide synthases)
RN 212839-30-0 CAPLUS
CN L-Norvaline, 5-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



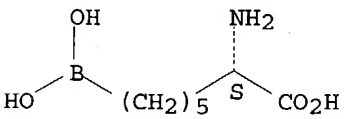
IT **222638-65-5P 266000-36-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and evaluation of enantiopure ω-borono-α-amino acids as inhibitors of arginase and nitric oxide synthases)
RN 222638-65-5 CAPLUS
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 266000-36-6 CAPLUS
CN Heptanoic acid, 2-amino-7-borono-, (2S)- (9CI) (CA INDEX NAME)

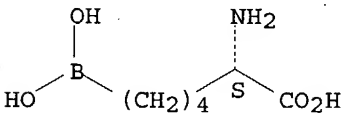
Absolute stereochemistry.



REFERENCE COUNT: 42
REFERENCE(S):
(1) Aoyagi, Y; Phytochemistry 1985, V24, P1835 CAPLUS
(2) Babu, B; Curr Opin Chem Biol 1998, V2, P491 CAPLUS
(3) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS
(4) Bajgrowicz, J; Tetrahedron Lett 1984, V25, P2231 CAPLUS
(6) Belokon, Y; J Am Chem Soc 1985, V107, P4252 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:799941 CAPLUS
DOCUMENT NUMBER: 132:148344
TITLE: A New Chromophoric Assay for Arginase Activity
AUTHOR(S): Baggio, Rick; Cox, J. David; Harper, Sandy L.; Speicher, David W.; Christianson, David W.
CORPORATE SOURCE: Roy and Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA
SOURCE: Anal. Biochem. (1999), 276(2), 251-253
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It is reported that 1-nitro-3-guanidinobenzene (NGB) is a new assay substrate for arginase, yielding products urea plus the chromophore m-nitroaniline. The simple two-step synthesis of NGB is outlined. The authors concluded with a description of its kinetic parameters and a brief discussion of the utility of this assay. (c) 1999 Academic Press.
IT **222638-65-5**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(chromophoric assay for arginase activity using nitroguanidinobenzene as substrate and study of enzyme inhibition by aminoboronohexanoic acid)
RN 222638-65-5 CAPLUS
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14
REFERENCE(S):
(2) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS
(3) Bergeron, R; J Org Chem 1987, V52, P1700 CAPLUS
(4) Bewley, M; Structure 1999, V7, P435 CAPLUS
(5) Cavalli, R; Biochemistry 1994, V33, P10652 CAPLUS
(6) Christianson, D; Prog Biophys Mol Biol 1997, V67, P217 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

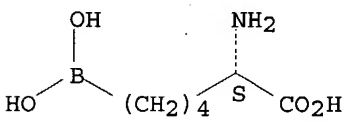
L9 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:725889 CAPLUS
DOCUMENT NUMBER: 132:76677
TITLE: Arginase-boronic acid complex highlights a physiological role in erectile function
AUTHOR(S): Cox, J. David; Kim, Noel N.; Traish, Abdulmaged M.; Christianson, David W.
CORPORATE SOURCE: Roy and Diana Vagelos Laboratories, Department of

Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA
SOURCE: Nat. Struct. Biol. (1999), 6(11), 1043-1047
CODEN: NSBIEW; ISSN: 1072-8368
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The crystal structure of the complex between the binuclear manganese metalloenzyme arginase and the boronic acid analog of L-arginine, 2(S)-amino-6-boronohexanoic acid (ABH), has been determined at 1.7 Å resolution from a crystal perfectly twinned by hemihedry. ABH binds as the tetrahedral boronate anion, with one hydroxyl oxygen sym. bridging the binuclear manganese cluster and a second hydroxyl oxygen coordinating to Mn2+A. This binding mode mimics the transition state of a metal-activated hydroxide mechanism. This transition state structure differs from that occurring in NO biosynthesis, thereby explaining why ABH does not inhibit NO synthase. We also show that arginase activity is present in the penis. Accordingly, the tight binding and specificity of ABH allows us to probe the physiol. role of arginase in modulating the NO-dependent smooth muscle relaxation required for erection. Strikingly, ABH causes significant enhancement of nonadrenergic, noncholinergic nerve-mediated relaxation of penile corpus cavernosum smooth muscle, suggesting that arginase inhibition sustains L-arginine concns. for NO synthase activity. Therefore, human penile arginase is a potential target for therapeutic intervention in the treatment of erectile dysfunction.

IT **222638-65-5D**, arginase complexes
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(arginase-boronic acid complex highlights a physiol. role in erectile function)
RN 222638-65-5 CAPLUS
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35
REFERENCE(S):
(1) Albina, J; J Immunol 1990, V144, P3877 CAPLUS
(3) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS
(4) Baggio, R; J Pharmacol Exp Ther 1999, V290, P1409 CAPLUS
(5) Bewley, M; Structure 1999, V7, P435 CAPLUS
(6) Brunger, A; Acta Crystallogr 1998, VD54, P905 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:547966 CAPLUS
DOCUMENT NUMBER: 131:295396
TITLE: Biochemical and functional profile of a newly developed potent and isozyme-selective arginase inhibitor
AUTHOR(S): Baggio, Ricky; Emig, Frances A.; Christianson, David W.; Ash, David E.; Chakder, Sushanta; Rattan, Satish
CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, USA
SOURCE: J. Pharmacol. Exp. Ther. (1999), 290(3), 1409-1416

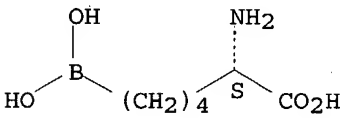
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An increase in arginase activity has been associated with the pathophysiol. of a number of conditions, including an impairment in nonadrenergic and noncholinergic (NANC) nerve-mediated relaxation of the gastrointestinal smooth muscle. An arginase inhibitor may rectify this condition. We compared the effects of a newly designed arginase inhibitor, 2(S)-amino-6-boronohexanoic acid (ABH), with the currently available Nω-hydroxy-L-arginine (L-HO-Arg), on the NANC nerve-mediated internal anal sphincter (IAS) smooth-muscle relaxation and the arginase activity in the IAS and other tissues. Arginase caused an attenuation of the IAS smooth-muscle relaxations by NANC nerve stimulation that was restored by the arginase inhibitors. L-HO-Arg but not ABH caused dose-dependent and complete reversal of Nω-nitro-L-arginine-suppressed IAS relaxation that was similar to that seen with L-arginine. Both ABH and L-HO-Arg caused an augmentation of NANC nerve-mediated relaxation of the IAS. In the IAS, ABH was found to be ≈250 times more potent than L-HO-Arg in inhibiting the arginase activity. L-HO-Arg was found to be 10 to 18 times more potent in inhibiting the arginase activity in the liver than in nonhepatic tissues. We conclude that arginase plays a significant role in the regulation of nitric oxide synthase-mediated NANC relaxation in the IAS. The advent of new and selective arginase inhibitors may play a significant role in the discrimination of arginase isoenzymes and have important pathophysiol. and therapeutic implications in gastrointestinal motility disorders.

IT **222638-65-5**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biochem. and functional profile of potent and isoenzyme-selective arginase inhibitor, 2(S)-amino-6-boronohexanoic acid)

RN 222638-65-5 CAPLUS
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 43
REFERENCE(S):
(1) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS
(2) Biancani, P; Gastroenterology 1985, V89, P867 CAPLUS
(3) Boucher, J; Biochem Biophys Res Commun 1994, V203, P1614 CAPLUS
(4) Buga, G; Am J Physiol 1996, V271, PH1988 CAPLUS
(5) Cavalli, R; Biochemistry 1994, V33, P10652 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:271330 CAPLUS
DOCUMENT NUMBER: 130:282369
TITLE: Preparation of borono amino acids as arginase inhibitors
INVENTOR(S): Christianson, David W.; Baggio, Ricky; Elbaum, Daniel
PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9919295	A1	19990422	WO 1998-US21430	19981009
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9897979	A1	19990503	AU 1998-97979	19981009
PRIORITY APPLN. INFO.:			US 1997-61607	19971010
			WO 1998-US21430	19981009

OTHER SOURCE(S): MARPAT 130:282369
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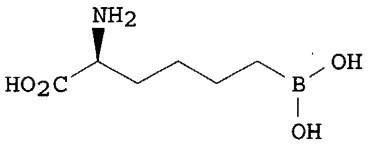


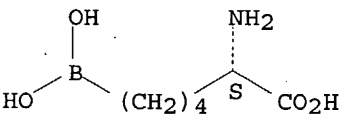
II

AB Title compds. HO2CCH(NH2)-Y1-Y2-Y3-Y4-B(OH)2 (I; Y1-Y4 = independently CH2, S, O, NH, N-alkyl; with the proviso that Y2 ≠ S when Y1 = Y3 = Y4 = CH2) are described. Compns. and methods for inhibiting arginase activity using I, including arginase activity in a mammal, are provided. Methods of making the compns. of the invention are also provided as are methods of using the compns. therapeutically. Thus, borono amino acid II, prepared in 5 steps from Boc-Glu-OCMe3 via conversion to the side chain aldehyde, Wittig olefination with Ph3P:CH2, hydroboration with BH3, trapping with (1S,2S,4R,6S)-(+)-pinanediol, and deprotection with BCl3, inhibited arginase with Ki = 0.1 μM.

IT **194656-75-2P**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of borono amino acids as arginase inhibitors)

RN 194656-75-2 CAPLUS
CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

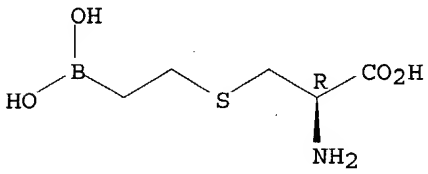


● HCl

IT **63107-40-4P 212839-31-1P 222638-65-5P 222638-67-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of borono amino acids as arginase inhibitors)

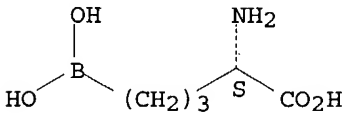
RN 63107-40-4 CAPLUS
CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 212839-31-1 CAPLUS
CN L-Norvaline, 5-borono-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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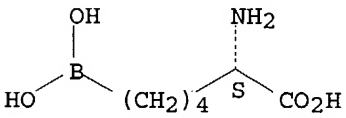
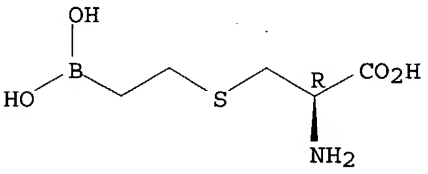
RN 222638-65-5 CAPLUS
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 222638-67-7 CAPLUS
CN L-Cysteine, S-(2-boronoethyl)-, hydrochloride (9CI) (CA INDEX NAME)

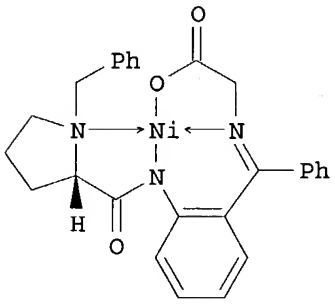
Absolute stereochemistry.



● HCl

REFERENCE COUNT: 2
REFERENCE(S):
(1) Baggio, R; J Am Chem Soc 1997
(2) Denniel, V; Tetrahedron Lett 1996

L9 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:482481 CAPLUS
DOCUMENT NUMBER: 129:230968
TITLE: Stereoselective, nonracemic synthesis of ω-borono-α-amino acids
AUTHOR(S): Collet, Sylvain; Bauchat, Patrick; Danion-Bougot, Renee; Danion, Daniel
CORPORATE SOURCE: Synthese et Electrosynthese Organiques, UMR 6510, Universite de Rennes I, Rennes, 35042, Fr.
SOURCE: Tetrahedron: Asymmetry (1998), 9(12), 2121-2131
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:230968
GI



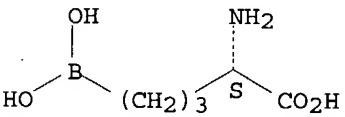
I

AB ω-Unsatd. α-amino acids are synthesized through condensation of allyl and propargyl bromides or of 9-bromoundecene with glycinate Schiff base Ni(II) complex I. Hydroboration with diisopinocampheylborane followed by oxidation with acetaldehyde affords enantiomerically pure ω-borono-α-aminocarboxylic acids.

IT **212839-30-0P 212839-31-1P 212839-32-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective, nonracemic synthesis of borono amino acids via preparation and hydroboration of unsatd. amino acids)

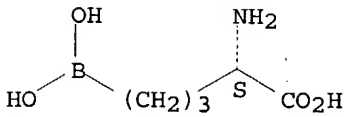
RN 212839-30-0 CAPLUS
CN L-Norvaline, 5-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 212839-31-1 CAPLUS
CN L-Norvaline, 5-borono-, hydrochloride (9CI) (CA INDEX NAME)

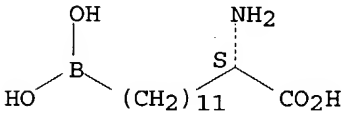
Absolute stereochemistry.



● HCl

RN 212839-32-2 CAPLUS
CN Tridecanoic acid, 2-amino-13-borono-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L9 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:528761 CAPLUS
DOCUMENT NUMBER: 127:201930
TITLE: Inhibition of Mn2+2-arginase by borate leads to the design of a transition state analog inhibitor, 2(S)-amino-6-boronohexanoic acid
AUTHOR(S): Baggio, Ricky; Elbaum, Daniel; Kanyo, Zoltan F.; Carroll, Patrick J.; Cavalli, R. Christopher; Ash, David E.; Christianson, David W.
CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA
SOURCE: J. Am. Chem. Soc. (1997), 119(34), 8107-8108
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The tetrahedral borate anion is a modest inhibitor of Mn2+2-arginase, a critical metalloenzyme of mammalian nitrogen metabolism The crystal structure of the arginase-ornithine-borate complex reveals the net displacement of the solvent mol. bridging the binuclear manganese cluster by a borate oxygen atom in the native enzyme active site. Since this binding mode is reminiscent of the tetrahedral intermediate proposed for arginase-catalyzed arginine hydrolysis, it is postulated that a boronic acid-based arginine isostere would bind to arginase as the tetrahedral boronate anion and therefore mimic the tetrahedral intermediate and its flanking transition states in catalysis. Arginine isostere 2(S)-amino-6-boronohexanoic acid (I) was synthesized and evaluated for inhibition of arginase-catalyzed arginine hydrolysis. The results indicate that I is one of the most potent reversible inhibitors of arginase known to date with IC50 = 0.8 μM. Complete kinetic characterization of I is complicated by nonlinearity of unknown origin (there is no evidence for slow-binding behavior), but competition binding expts. with N-hydroxyarginine indicate that Kd ≤ 0.1 μM. Based on anal. of the crystal structure of the arginase-ornithine-borate

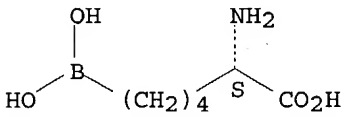
complex, a possible binding mode for I is postulated in which the metal-bridging solvent mol. observed in the native enzyme is displaced by an oxygen atom of the tetrahedral boronic acid anion.

IT **194656-75-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

RN 194656-75-2 CAPLUS

CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L9 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1996:454874 CAPLUS

DOCUMENT NUMBER: 125:222375

TITLE: Hydroboration of vinylglycine and allylglycine as a route to boron-derivatives of α-amino acids

AUTHOR(S): Denniel, Valerie; Bauchat, Patrick; Danion, Daniel; Danion-Bougot, Renee

CORPORATE SOURCE: Groupe Rech. Physicochim. Struct., Univ. Rennes I, Rennes, 35042, Fr.

SOURCE: Tetrahedron Lett. (1996), 37(29), 5111-5114
CODEN: TELEAY; ISSN: 0040-4039

DOCUMENT TYPE: Journal

LANGUAGE: English

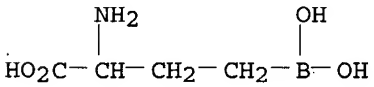
OTHER SOURCE(S): CASREACT 125:222375

AB The hydroboration of protected vinylglycine and allylglycine with dicyclohexyl- or diisopinocampheylborane occurs chemo- and regioselectively with attachment of boron to the less substituted end of the C:C double bond. Homoserine or δ-hydroxynorvaline are readily obtained by H2O2/AcONa oxidation of dicyclohexylborane derivs. and 2-amino-4-boronobutanoic acid or 2-amino-5-boronopentanoic acid by reaction of diisopinocampheylborane derivs. with excess of acetaldehyde and deprotection.

IT **181312-07-2P 181312-08-3P 181312-09-4P 181312-10-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(hydroboration of vinylglycine and allylglycine in preparation of borono amino acids)

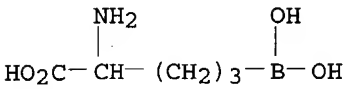
RN 181312-07-2 CAPLUS

CN Butanoic acid, 2-amino-4-borono-, hydrochloride (9CI) (CA INDEX NAME)

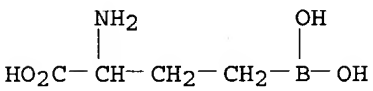


● HCl

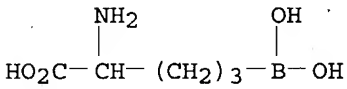
RN 181312-08-3 CAPLUS
CN Norvaline, 5-borono-, hydrochloride (9CI) (CA INDEX NAME)



RN 181312-09-4 CAPLUS
CN Butanoic acid, 2-amino-4-borono- (9CI) (CA INDEX NAME)



RN 181312-10-7 CAPLUS
CN Norvaline, 5-borono- (9CI) (CA INDEX NAME)



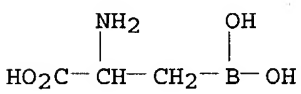
L9 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1990:77900 CAPLUS
DOCUMENT NUMBER: 112:77900
TITLE: Analogs of carbamyl aspartate as inhibitors of dihydroorotase: preparation of boronic acid transition-state analogs and a zinc chelator carbamylhomocysteine
AUTHOR(S): Kinder, David H.; Frank, Sandra K.; Ames, Matthew M.
CORPORATE SOURCE: Dep. Oncol., Mayo Clin. Found., Rochester, MN, 55905, USA
SOURCE: J. Med. Chem. (1990), 33(2), 819-23
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 112:77900

AB Dihydroorotase (DHO) catalyzes the conversion of carbamylaspartate (CA) to dihydroorotate (DO) in the de novo pyrimidine biosynthetic pathway. Utilizing 2 mechanism-based strategies, we have designed and prepared potential DHO inhibitor analogs of CA. One strategy replaced the side-chain carboxyl moiety of CA with a boronic acid. This substitution yields compds. which form stable charged tetrahedral intermediates and mimic the enzyme-substrate transition state. Preparation of the boronic acid analogs of CA and its carboxylic acid esters focused on a Curtius rearrangement as a key step following a malonic ester synthesis. This was followed by carbamoylation of the free amine under nonaq. neutral conditions with Si(NCO)4. The Et ester was a competitive inhibitor of DHO with an apparent Ki of 5.07 μM, while the nonesterified analog and the Me ester were not effective inhibitors. None of the compds. were

cytotoxic against L1210 cells in culture. An active-site-directed sulfhydryl-containing zinc chelator was also prepared This analog irreversibly inhibited the enzyme, but it also was ineffective in L1210 growth inhibition.

IT **108082-89-9**
RL: RCT (Reactant)
(carbon-14-labeled carbamoylation of)

RN 108082-89-9 CAPLUS
CN Alanine, 3-borono- (9CI) (CA INDEX NAME)

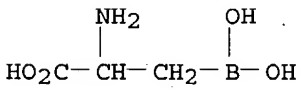


L9 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1987:407557 CAPLUS
DOCUMENT NUMBER: 107:7557
TITLE: Synthesis of 2-amino-3-boronopropionic acid: a boron-containing analog of aspartic acid
AUTHOR(S): Kinder, David H.; Ames, Matthew M.
CORPORATE SOURCE: Dep. Oncol., Mayo Clin. Found., Rochester, MN, 55905, USA
SOURCE: J. Org. Chem. (1987), 52(12), 2452-4
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 107:7557

AB The boron-containing analog of aspartic acid, 2-amino-3-boronopropionic acid, in which the side chain carboxyl group has been replaced by a boronic acid group, was prepared by two principal reactions: a malonic ester alkylation with (chloromethyl)boronic esters, and, after saponification of one Et ester of the adduct, a modified Curtius rearrangement to introduce the amino group. Unlike α-amino boronic esters, the primary β-amino boronic acids and esters reported are stable and do not undergo elimination reactions.

IT **108082-89-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 108082-89-9 CAPLUS
CN Alanine, 3-borono- (9CI) (CA INDEX NAME)

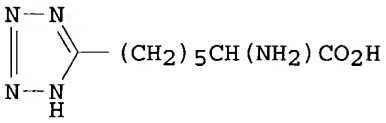


L9 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1983:198451 CAPLUS
DOCUMENT NUMBER: 98:198451
TITLE: Isomeric amino acids and their use in medicine
PATENT ASSIGNEE(S): City of London Polytechnic, UK
SOURCE: Belg., 23 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 894116	A1	19830214	BE 1982-208817	19820813
SE 8204640	A	19830215	SE 1982-4640	19820810
NL 8203167	A	19830301	NL 1982-3167	19820812
FR 2511378	A1	19830218	FR 1982-14108	19820813
FR 2511378	B1	19860124		
GB 2104078	A	19830302	GB 1982-23363	19820813
GB 2104078	B2	19850123		
CH 656613	A	19860715	CH 1982-4869	19820813
JP 58131957	A2	19830806	JP 1982-141586	19820814

PRIORITY APPLN. INFO.: GB 1981-24899 19810814

GI



I

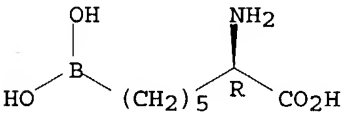
AB (-)-D-Isomers of XQCH(NHR)CO2R1 [Q = (un)substituted C5 aliphatic radical; X = acid radical; R, R1 = lipophilic radical, H, salts or pharmaceutically acceptable bioprecursors] were prepared by standard methods and exhibited anticonvulsant activity (no data). Thus, treating the Na salt of di-Et phosphite with 1,5-dibromopentane gave Br(CH2)5P(O)(OEt)2. Treating the latter with the Na salt of AcNHCH(CO2Et)2, followed by acid hydrolysis, gave (±)-H2O3P(CH2)5CH(NH2)CO2H. The latter was resolved by use of L-lysine. Also prepared were (-)-HO3S(CH2)5CH(NH2)CO2H, (-)-I, and (-)-(HO)2B(CH2)5CH(NH2)CO2H.

IT **85685-94-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and formation of lipophilic anticonvulsants from)

RN 85685-94-5 CAPLUS

CN Heptanoic acid, 2-amino-7-borono-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1977:406321 CAPLUS

DOCUMENT NUMBER: 87:6321

TITLE: Preparation and evaluation of immunoglobulins labeled with S-(2-boronoethyl)cysteine

AUTHOR(S): Hartz, Thomas Peter, Jr.

CORPORATE SOURCE: Memphis State Univ., Memphis, Tenn., USA

SOURCE: (1976) 87 pp. Avail.: Xerox Univ. Microfilms, Ann Arbor, Mich., Order No. 77-3150
From: Diss. Abstr. Int. B 1977, 37(8), 3927-8

DOCUMENT TYPE: Dissertation

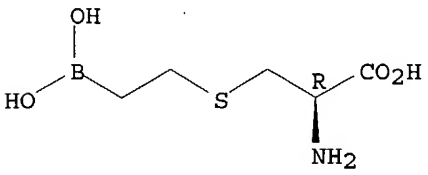
LANGUAGE: English

AB Unavailable

IT **63107-40-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)

(labeling of immunoglobulins with, preparation and evaluation of)
RN 63107-40-4 CAPLUS
CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d it 12

L9 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2000 ACS
IT Immunoglobulins
RL: SPN (Synthetic preparation); PREP (Preparation)
(labeled with (boronethyl)cysteines, preparation and evaluation of)
IT **63107-40-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(labeling of immunoglobulins with, preparation and evaluation of)

=> s l9 and arginase

2722 ARGINASE
113 ARGINASES
2723 ARGINASE
(ARGINASE OR ARGINASES)
L10 6 L9 AND ARGINASE

=> d ti 1-6

L10 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2000 ACS
TI Synthesis and evaluation of ω-borono-α-amino acids as active-site probes of **arginase** and nitric oxide synthases

L10 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2000 ACS
TI A New Chromophoric Assay for **Arginase** Activity

L10 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2000 ACS
TI **Arginase**-boronic acid complex highlights a physiological role in erectile function

L10 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2000 ACS
TI Biochemical and functional profile of a newly developed potent and isozyme-selective **arginase** inhibitor

L10 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2000 ACS
TI Preparation of borono amino acids as **arginase** inhibitors

L10 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2000 ACS
TI Inhibition of Mn2+2-**arginase** by borate leads to the design of a transition state analog inhibitor, 2(S)-amino-6-boronohexanoic acid

=> file beilstein

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FILE LAST UPDATED: 6 MAR 2000

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*** FILE CONTAINS 7,688,486 SUBSTANCES ***

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SCREENING
FULL SCREEN SEARCH COMPLETED -      17 TO ITERATE

100.0% PROCESSED      17 ITERATIONS                                 4 ANSWERS
SEARCH TIME: 00.00.35

L11            4 SEA SSS FUL L1

=> d ide 4


L11  ANSWER 4 OF 4  COPYRIGHT 2000 BEILSTEIN CDS MDL

Beilstein Reg. No. (BRN):   3141428  Beilstein
Molecular Formula (MF):     C9 H12 B N O4
Chemical Name (CN):         4-dihydroxyboranyl-phenylalanine
                            4-Dihydroxyboryl-phenylalanin
Beilstein Reference (SO):   4-16-00-01688
CAS Reg. No. (RN):          76410-58-7; 77374-29-9; 90580-64-6; 111821-49-9
Rltd. Stereoisomers (RSI):  4458616
Formula Weight (FW):        209.01
Lawson Number (LN):         16761
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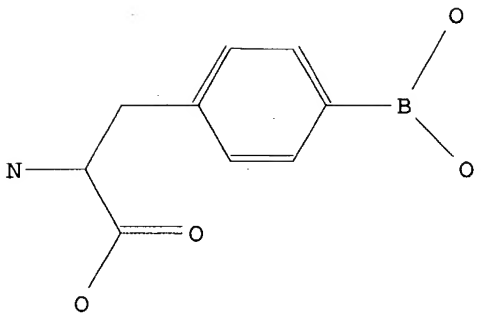


=> d ide 3

L11 ANSWER 3 OF 4 COPYRIGHT 2000 BEILSTEIN CDS MDL

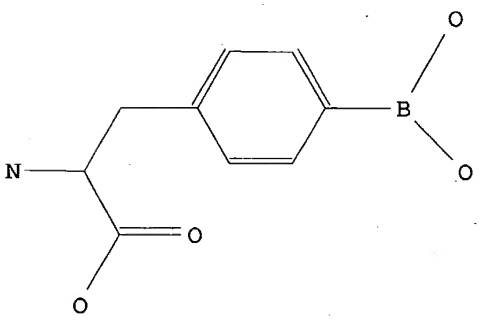
Beilstein Reg. No. (BRN): 3733224 Beilstein
Molecular Formula (MF): C9 H12 B N O4 . (x) Cl H
Lin. Struct. Formula (LSF): C9H12BNO4*(x)HCl
Chemical Name (CN): 4-dihydroxyboranyl-phenylalanine ; hydrochloride
4-Dihydroxyboryl-phenylalanin; Hydrochlorid
Beilstein Reference (SO): 4-16-00-01688
CAS Reg. No. (RN): 76410-59-8; 91196-68-8; 112725-17-4

Component Data:

Component Reg. No. (CBRN)	Component Molec. Formula (CMF)	Formula Weight (FW)	Lawson Number (LN)
3141428	C9 H12 B N O4	209.01	16761
1098214	Cl H	36.46	

CM 1

CBRN 3141428
CMF C9 H12 B N O4



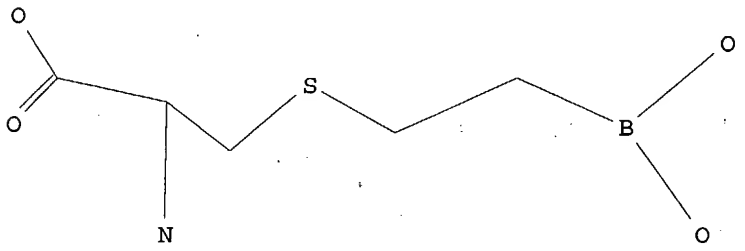
CM 2

CBRN 1098214
CMF Cl H

=> d ide 2

L11 ANSWER 2 OF 4 COPYRIGHT 2000 BEILSTEIN CDS MDL

Beilstein Reg. No. (BRN): 4132291 Beilstein
Molecular Formula (MF): C5 H12 B N O4 S
Synonym (SY): S-<2-Borono-aethylthio>-cyctein
Beilstein Reference (SO): 5-04
CAS Reg. No. (RN): 63107-40-4; 88642-86-8
Formula Weight (FW): 193.02
Lawson Number (LN): 3813; 3544



=> d pre 2

L11 ANSWER 2 OF 4 COPYRIGHT 2000 BEILSTEIN CDS MDL

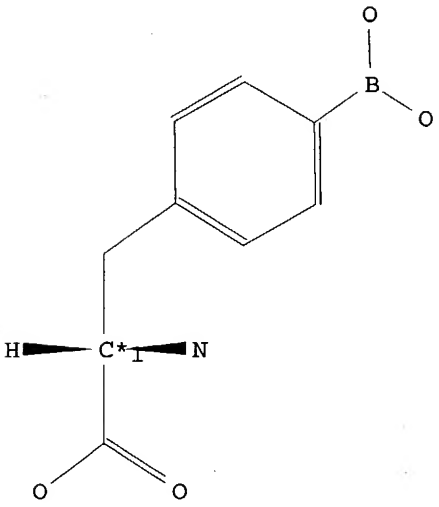
Preparation:
PRE
Start: BRN=1721406 cysteine, BRN=1768115 dibutoxy-vinyl-borane
Solv: methanol, H2O
Heating
Reference(s):
1. Matteson,D.S. et al., J.Med.Chem., 7 <1964>, 640-643, LA: EN, CODEN: JMCMAR

=> d ide 1

L11 ANSWER 1 OF 4 COPYRIGHT 2000 BEILSTEIN CDS MDL

Beilstein Reg. No. (BRN): 4458616 Beilstein
Molecular Formula (MF): C9 H12 B N O4
Synonym (SY): L-p-dihydroxyborylphenylalanine
Beilstein Reference (SO): 6-16
General Comments (NTE): Stereo compound
CAS Reg. No. (RN): 76410-58-7; 77374-29-9; 90580-64-6; 111821-49-9

Rltd. Stereoisomers (RSI): 3141428
Formula Weight (FW): 209.01
Lawson Number (LN): 16761



Atom/Bond Notes:
1. CIP Descriptor: S

=> file caplus